BRITISH JOURNAL OF TUBERCULOSIS
AND DISEASES OF THE CHEST
Vol. LII. JANUARY, 1958 No. 1.

EDITORIAL

THIS issue inaugurates the fifty-second year of publication of this Journal. It has covered a period when the advances in the realm of intrathoracic disease and its changing pattern have been quite outstanding. The newer outlook on the prevention and treatment of pulmonary tuberculosis, the challenge presented by chronic bronchitis in this country where the mortality rate is at least twenty times as great as in Scandinavia, and the gauntlet thrown to medical workers by cancer of the lung, are all problems to be overcome. Extending knowledge of the lungs in heart disease, of the heart in chronic pulmonary disease, and the surgery of heart disease, as well as that of lung disease, must be the preoccupation of those whose special interest lies in this sphere.

It will be seen from these few examples that the Journal has always to recognise its increasingly wide purview and that knowledge of diseases of the chest demands a wide conception embracing diseases of the heart, lungs and mediastinum, integrated with general medicine.

It is the policy of the Editorial Board not to lose sight of this concept, as is made manifest by the varied contributions to this issue.

Certain changes in the Editorial Board have been made during the year. The first creates a new and welcome precedent, namely an Assistant Editor in the person of Mr. J. R. Belcher, whose contributions to thoracic surgery require no introduction.

As has already been recorded, we have lost the services, through retirement, of three stalwarts, namely Professor Charles Cameron, Dr. Maurice Davidson and Dr. Reginald Ellis. We remain greatly indebted to them for past services. We welcome in their place Dr. Frank Scadding, Dr. I. W. B. Grant and Dr. R. Y. Keers. Professor O. L. Wade, of the Department of Pharmacology of the University of Belfast, is welcomed as an important representative on the Editorial Board of this aspect of our work. Representation from the dominions remains unchanged.

Finally, we would appeal to our contributors, in view of the tremendous pressure on our space, to conform to the Notice to Contributors on the inside back cover of the Journal and to present their manuscripts in conformity with the style of this Journal, recognising the importance of vigorous pruning in the interests of its reputation and the responsibility to its readers.

THE USE OF INSPIRATORY POSITIVE PRESSURE BREATHING IN CARDIO-PULMONARY DISEASES

By Frank D. Gray, Jr., and Shirley R. MacIver

From the Department of Internal Medicine and the Cardio-pulmonary Laboratory, Yale University School of Medicine, New Haven, Conn.

Inspiratory positive pressure breathing (IPPB) has been developed from the early pressure breathing studies of Barach *et al.* (1938). It is a form of mechanical ventilation which has become an important type of therapy in cardio-pulmonary diseases following the careful work of Barach, Fenn, Ferris, and Schmidt (1947) and Motley *et al.* (1948 a and b). Its chief value has been found in treating acute pulmonary oedema and a variety of chronic lung diseases.

Rationale of IPPB

In addition to the well-known tank and cuirass ventilators, several kinds of mechanical ventilation are currently being used. Resuscitators provide automatically cycled inspiratory positive pressure and expiratory negative pressure at the mouth and require no effort from the patient. These devices are used chiefly in asphyxial states, and probably have no place in the long-term therapy of chronic cardio-pulmonary diseases. Demand regulated positive pressure equipment, in which the patient initiates the respiratory cycle, provides either continuous positive pressure (CPPB) in which inspiration and expiration are both affected while the mouth pressure remains positive, or intermittent positive pressure. Intermittent expiratory positive pressure (EPPB) implies some form of resistance to expiratory air flow, and intermittent inspiratory positive pressure breathing (IPPB) refers to the technique of ventilating a patient with positive pressure during inspiration, expiration proceeding at atmospheric pressure. CPPB and EPPB will not be given further consideration as they require excessive effort on the part of the patient, and lead to considerable circulatory derangement (Werko, 1947).

The circulatory consequences of positive pressure breathing have been clearly described (Werko, 1947) and consist in a fall in cardiac output, and a rise in peripheral venous pressure. These effects follow the diminished venous return resulting from a rise in the mean intrathoracic pressure. The change in cardiac output varies from zero to 39 per cent. below the initial level in men on IPPB, and up to a 60 per cent. reduction in dogs. The effects of IPPB on ventilation are less clear. The minute volume is usually increased with an ensuing increase in arterial blood oxygen saturation, and pH, and decrease in arterial blood carbon dioxide tension (Motley *et al.*, 1948a). However, the mechanisms underlying prolonged improvement in patients

(*Received for publication, September* 23, 1957.)

with chronic bronchitis and emphysema are obscure, and the immediate effect in some patients may suggest impaired rather than improved function.

Clinical Application of IPPB

Patients regularly produce more sputum while undergoing IPPB therapy, and this may be the result of an accentuation of the normal mechanism for clearing bronchial exudates and secretions. The overdistension that occurs during treatment (Gray *et al.*, 1955) could serve to open obstructed bronchioles or to expand collapsed broncho-pulmonary segments.

Although IPPB is used most often in pulmonary emphysema or asthma, it may also be used in the management of acute pulmonary oedema. In this situation its effectiveness is the result of decreased venous return consequent upon a raised mean intrathoracic pressure. Thus it is comparable with phlebotomy or tourniquets on the extremities. There is little reason to believe that increased inspiratory pressure actually pushes transudates back into pulmonary capillaries, since the increased pressure is almost equally distributed throughout the thoracic space and all contained organs, including heart and blood vessels, so that the actual increase in pressure gradient across the capillary membrane must be small indeed. There is some evidence that pulmonary vascular capacity is increased with greater distension (Ochsner, 1952) and that pulmonary vascular resistance increases (Edwards, 1951), both of which might protect the pulmonary capillaries from further injury in the case of increased capillary permeability. Expiratory positive pressure will raise the intrathoracic mean pressure also, thus impeding venous return, but it requires greater work on the part of the patient, whereas IPPB relieves him of work, and is, therefore, much to be preferred.

The patient who receives optimal benefit notices easier breathing, increased exercise tolerance, less wheezing, and easier production of sputum following treatment. The sputum is usually more copious. Although the immediate effect on tests of cardio-pulmonary function may be to increase, distension as indicated by a larger functional residual capacity, impaired intrapulmonary distribution of respiratory gases (Gray *et al.*, 1955), and lowered arterial blood oxygen saturation (Wilson, 1957), the long-term effect is an improvement in most or all of these functions. However, many patients with chronic pulmonary disease do not improve, and the determining factors are largely unknown. In general, patients showing evidence of pulmonary distension reflected by a large residual volume, even though considerable emphysema may be present, will improve. Included in this category would be patients with asthma, chronic bronchitis, so-called "idiopathic" emphysema, and bullous emphysema. In contrast, purely restrictive diseases with considerable fibrosis do not respond well. There have been many exceptions in both groups.

IPPB has also proved useful in administering oxygen to emphysematous patients with hypercapnoea and hypoxia who tolerate high concentrations of oxygen poorly yet need additional oxygen. It has been known for some time that administration of oxygen to these patients often leads to hypoventilation

or apnoea and an alarming increase in arterial blood carbon dioxide tension (Comroe, 1950). Apparently high serum bicarbonate of any type diminishes the respiratory centre's sensitivity to carbon dioxide (Alexander *et al.*, 1955); hence only the hypoxia acts as a ventilatory drive in these patients. Once oxygen inhalation removes the hypoxia, hypoventilation follows. However, these patients do very well on IPPB with oxygen since the hyperventilation that almost always occurs with IPPB reduces blood carbon dioxide while increasing blood oxygen, and the mechanical nature of the treatment precludes hypoventilation. Should complete apnoea occur, it is simple to maintain cycling by means of automatic attachments, or by operating a manual trigger for inspiration.

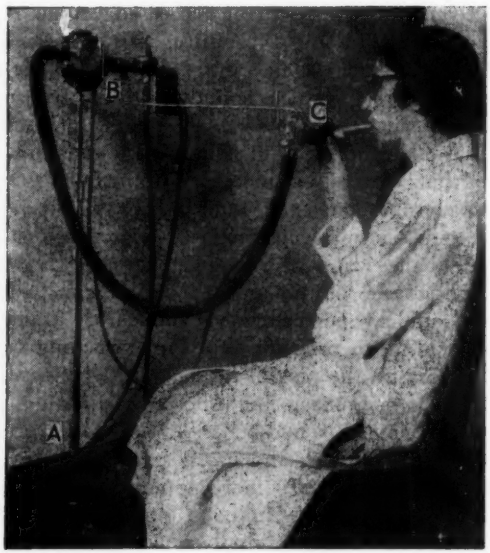

FIG. 1.—The Apparatus.

A—Air compressor pump. B—Flow valve assembly. C—Face valve assembly.

IPPB has been useful in the surgical recovery room as a means of preventing post-operative lobar or segmental collapse of the lung, especially following gall bladder surgery, and herniorrhaphies in older people. It may be used to prevent atelectasis in patients with poliomyelitis or other neurological problems involving respiratory paralysis and to ventilate such patients outside of tank respirators for nursing procedures, and examinations.

THE APPARATUS AND ITS USE

Several types of apparatus are presently available. Some are flow sensitive, others pressure sensitive. The latter are usually more rugged and will with-

TABLE 1.—LABORATORY AND CLINICAL DATA

Case number	Vital capacity (litres)		Functional residual capacity (litres)		Maximal breathing capacity (l./min.)		Arterial oxygen saturation (%)		Clinical status*
	Before	After	Before	After	Before	After	Before	After	
Diagnosis: Asthma									
1	3,545	4,623	6·07	†1·84	75	104	94	95	G.I.
2	4,322	4,239	7·97	6·59	67	65	95	95	M.I.
Diagnosis: Asthma, emphysema									
3	3,731	3,669	4·08	4·82	105	101	—	97	S.I.
4	3,586	3,607	2·58	6·28	60	62	—	89	M.I.
Diagnosis: Bronchitis, emphysema									
5	2,073	2,197	4·61	4·45	29	34	—	—	M.I.
6	2,123	1,866	3·95	3·67	45	41	84	90	G.I.
7	1,306	1,866	8·26	5·00	25	34	91	91	G.I.
8	2,819	1,969	6·03	4·25	47	34	97	95	M.I.
9	3,213	3,130	5·31	4·01	52	70	95	—	G.I.
10	1,099	1,741	7·76	3·00	22	21	89	92	S.I.
11	1,907	2,166	6·54	6·36	30	34	93	99	M.I.
12	2,197	1,969	4·85	4·04	36	39	91	88	S.I.
13	2,270	2,850	5·03	4·89	22	57	83	83	M.I.
14	705	819	3·28	3·27	17	21	—	87	M.I.
15	1,472	1,565	4·63	3·64	66	101	91	96	G.I.
16	1,669	1,721	6·30	6·90	24	20	92	95	W.
17	1,866	2,000	3·97	5·46	16	20	91	90	N.C.
18	1,700	2,135	2·62	3·19	31	50	95	95	G.I.
19	4,187	5,473	5·76	4·25	39	74	88	85	G.I.
Diagnosis: Emphysema, cor pulmonale									
20	2,913	2,799	5·34	6·23	36	35	90	88	W.
21	2,633	2,539	—	—	39	52	96	—	M.I.
Diagnosis: Fibrosis, emphysema									
22	1,990	3,783	8·37	6·89	51	143	88	95	G.I.
Diagnosis: Byssinosis									
23	1,617	1,565	—	—	30	22	—	—	S.I.
Diagnosis: Fibrothorax									
24	1,679	2,021	4·12	4·29	40	42	96	98	M.I.
Diagnosis: Berylliosis									
25	2,446	3,078	7·71	2·72	145	135	94	—	M.I.
Diagnosis: Sarcoidosis									
26	1,368	1,617	2·57	3·09	26	28	85	81	N.C.
Diagnosis: Kypho-scoliosis									
27	601	715	0·61	2·20	29	26	86	90	S.I.

* G.I.=greatly improved; M.I.=moderately improved; S.I.=slightly improved; N.C.=no change; W.=worse. See text for explanation.

† The unusual fall in FRC in this case could have been due, in part, to normal fluctuation of the disease.

stand more abuse but they are less sensitive, thus less adaptable to patients with muscular weakness, so that both types should be available. Either type will operate on compressed air or oxygen, and air compressor pumps may be obtained for some models (Fig. 1).

The actual schedule of treatment is highly variable and dictated by the needs of the patient. In general, three or four treatments of 20 minutes each are given daily, although out-patients may be given only one treatment each day because of the difficulty they find in travelling to and from the clinic. The apparatus is usually adjusted for 20 cm. of water peak pressure, and an aerosol is administered throughout the course of treatment. The aerosol may consist of plain water or a bronchodilator agent. Detergents and liquefying enzymes should not be administered simultaneously with IPPB as the excessive sputum production following such treatment may lead to asphyxiation. Instead, these agents should be administered immediately after IPPB. Dry gas, either oxygen or compressed air, should never be administered, because of the excessive drying of respiratory mucous membranes that occurs with such treatment. Treatment is administered in courses of three weeks with intervening rest periods.

Clinical Evaluation

Ideally, treatment in chronic lung disease should be reflected in a return towards normal of altered lung volumes, improvement of impaired dynamic function, and better respiratory gas exchange. However, the expression "chronic lung disease" comprises many different pathological entities, so that uniform objective criteria of successful treatment are hard to find.

Probably no single test of pulmonary function could be relied upon to give a fair evaluation of a therapeutic measure, the mechanism of which is as poorly understood as in the case of IPPB, and it is certainly illogical to condemn the treatment because all of the many types of chronic lung disease do not respond. Thus in a heterogeneous group of 27 patients with several types of lung disease (our first cases in which this form of treatment was used) who received only IPPB administered by compressed air, 9 were improved in most tests of lung function, and one was worse in most tests (Table 1). Fourteen of the patients improved in at least one of the tests, but 7 of these were also worse in at least one test, and 3 were worse in one test with no change in the other tests.

A clinical estimation was attempted on the basis of exercise tolerance and cough.* Using these admittedly inexact criteria, 8 were found to be greatly improved, 10 moderately improved, 5 slightly improved, whereas 2 showed no change, and 2 were worse. No consistent relationship was apparent between changes in pulmonary function tests and clinical status.

* Increasing stair climbing tolerance two-fold was considered moderate improvement. Cough was considered greatly improved if the patient no longer noted cough, slightly improved if he noted less cough but still felt that it was a major disability.

Case Examples

The lack of parallel between laboratory tests and clinical findings is illustrated by a patient who was symptomatically improved after one course of treatment in spite of a rise in functional residual capacity (see patient number 18, Table 1). He had experienced dyspnoea on walking 20 feet before treatment. After treatment he had no dyspnoea on climbing 1 flight of stairs or walking one-half mile. This 60-year-old man had a long history of bronchitis with chronic cough. After the first series of IPPB treatments administered by compressed air, an aerosol of racemic epinephrine, breathing exercises, and postural drainage were added to his regimen with gradual reduction of his functional residual capacity to normal, until finally he became virtually symptom-free.

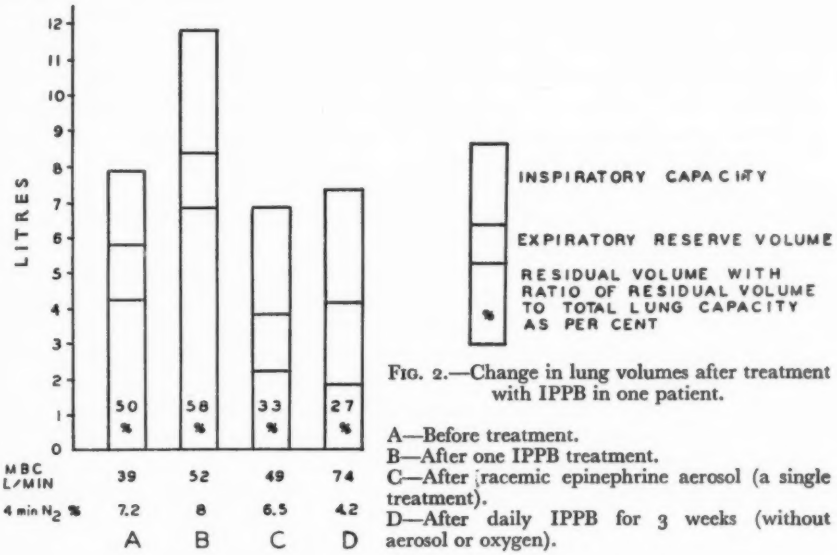

Fig. 2.—Change in lung volumes after treatment with IPPB in one patient.

A—Before treatment.
B—After one IPPB treatment.
C—After racemic epinephrine aerosol (a single treatment).
D—After daily IPPB for 3 weeks (without aerosol or oxygen).

The progress of another patient (number 19, Table 1 and Fig. 2), illustrates the course when optimal benefits are obtained. This patient, a 30-year-old farmer, had noted increasing exertional dyspnoea over a 2-year period. On the advice of his physician he stopped smoking, with relief of a chronic non-productive cough and some improvement in breathing, but he was still almost completely disabled. Pulmonary function studies revealed distension, hypoxemia, venous admixture, impaired intrapulmonary gas distribution, and impaired dynamic function. Immediately after his first IPPB treatment he felt subjectively better and could walk with less ventilatory effort, but his functional residual capacity rose, arterial blood oxygen saturation dropped and intrapulmonary gas distribution became worse. The maximal breathing capacity, however, rose significantly. After a 3 weeks' course of treatment all

functions were improved, and following his second course of treatment he was able to resume his work as a farmer. However, he continues to require periodic treatment.

Although in general patients with restrictive disease do not seem to gain much from IPPB, they may occasionally improve because of better mobility of the lung. Thus 3 of the patients in this series who had extensive fibrosis (number 22, 24, and 25, Table 1) showed clinical improvement as well as some improvement in pulmonary function tests.

Complications and Contra-indications

Over 20,000 individual treatments have been administered to about 500 patients since this form of treatment was first used in our institution. In addition, some 57 patients have purchased their own apparatus and have been administering their own treatment for up to four years. In this experience there have been two adverse reactions. The first, reported elsewhere (Gray, 1956), an elderly patient with kypho-scoliosis and heart disease developed very rapid and severe congestive heart failure within a few hours after treatment was begun.* Since cardiac output falls and peripheral venous pressure rises during IPPB, this phenomenon was not unexpected but apparently it is rare. Many of our other patients had evidence of congestive heart failure, but showed no ill effects after starting IPPB.

The other adverse reaction occurred in a young woman with a hæmolytic Staphylococcus aureus pneumonia who developed acute pulmonary œdema. In an effort to treat the acute pulmonary œdema, IPPB was used, but as she did not respond to the usual pressure of 20 cm. H_2O, it was raised to 40 cm. H_2O at which time evidence of pulmonary œdema disappeared but shortly after it was found that she had developed pneumothorax on the side of the pneumonia. This was but the beginning of a deplorable sequence involving empyema, eventually resection and thoracoplasty. Although the pneumothorax may have had no relation to the IPPB, it seems likely that the latter caused it.

In addition to these hazards, there is the theoretical possibility of shock because of diminished venous return, and, as has already been pointed out, of carbon dioxide narcosis in patients with hypercapnoea. The respiratory centre in these patients may be insensitive to carbon dioxide and respond only to anoxia. Even using compressed air with mechanical ventilation might overcome the hypoxia. As long as the IPPB is continued there would be little danger since the mechanical ventilation would maintain adequate gas exchange, but following cessation of treatment hypoventilation might ensue with resulting carbon dioxide narcosis. Since many of our patients have had very high carbon dioxide levels and this phenomenon has not been observed following IPPB therapy, it does not seem to be a very great hazard, and, of course, it could be averted by maintaining the IPPB until the carbon dioxide sensitivity of the respiratory centre returned.

* This was not the same patient as number 27 on Table 1 who also had kypho-scoliosis.

Tomashefski and Tchen (1955) have used IPPB in active pulmonary tuberculosis together with adequate antimicrobial therapy with no apparent danger from spread of infection or delayed healing.

Discussion

Miller, Fowler, and Helmholz (1955) and Wu and his associates (1955) have concluded that IPPB alone has little value. However, the former authors did find some improvement in a few patients and seem to have rejected the treatment on the grounds that uniform success was not met in all types of lung disease whereas the second group studied their patients for only short periods after a single treatment. Many of the patients included in the present report have, at first, appeared to be actually worse. Only after three weeks or more of treatment has improvement appeared in some cases, hence a study of the effect immediately after a treatment as in the case of the Wu report, could be misleading. Further, one should not expect that all patients with chronic lung disease would improve on a single type of treatment. This would be analagous to expecting all types of heart disease to improve upon administering digitalis.

The 27 patients entered in Table 1 were well known to our clinic and had reasonably stable disease. They received only IPPB and compressed air, neither oxygen nor aerosol being added. Thus improvement, when it occurred, was either spontaneous, which was unlikely, or induced solely by IPPB. The results were not startling, but they suggested that a new form of treatment with definite value and very little hazard was at hand, not as a replacement for all other therapy, but rather as a supplement.

Summary

In summary, inspiratory positive pressure breathing (IPPB) by itself and independently has therapeutic value, particularly in asthma, bronchitis and emphysema. It probably accomplishes this result by helping to clear the bronchial airways of obstructing secretions and exudations, although other effects as yet unknown may be important. The therapeutic results are erratic and the use of IPPB is justified only by the otherwise inexorable progress to an asphyxial death of crippling chronic pulmonary disease.

The technique may also be used as a means of temporarily diminishing venous return in acute pulmonary œdema, and of expanding collapsed segments of lung in respiratory paralysis and post-operative immobilisation of the lung. The hazards of this form of treatment are slight.

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CHRONIC BRONCHITIS AND OCCUPATION

By Ronald E. Lane

Department of Occupational Health, University of Manchester

A workman makes constant physical contact with his environment through two surfaces—his skin and respiratory tract—and both are liable to damage from that environment. Damage to the skin is frequent and obvious and it is not surprising that dermatitis resulting from the action of primary irritants or sensitising substances is the commonest of all industrial diseases, occurring more often than all others put together. Damage to the respiratory tract is probably less common, less easily detected and less readily attributable to a specific cause. While the immediate effects of an acute irritant are obvious, other substances have an insidious action and the real cause of a chronic affection of the respiratory tract may be obscure. During the last fifty years the nature of occupational respiratory disease has become much clearer. Radiography made it possible to identify the fibrosing conditions and emphasised the part frequently played by tuberculosis as a complicating factor in these conditions. In this way silicosis, asbestosis, coal miners' pneumoconiosis and other conditions have been identified, and it has been possible to attribute them to specific types of dust. Following this advance some workers appear to have assumed that all occupational damage to the chest could be demonstrated by X-ray. But it is now recognised that men whose chests appear normal on radiographic examination may well be disabled as the result of respiratory damage sustained at their work. That this should need stating is perhaps strange when one remembers the work of men like Arlidge and Collis fifty years ago. To re-read the Milroy Lectures given by Collis in 1915 is a salutary exercise for anyone working in this field. Collis had a vast experience of industry in the early years of the century, when working conditions were often bad, and there is no doubt that he was convinced of the important part occupational dusts could play in the production of chronic bronchitis.

The whole problem of chronic bronchitis has recently received wide attention, but it is proving difficult to investigate and progress is slow. This is inevitable in a disease in which diagnosis must rest entirely on a history of common symptoms—cough with sputum, wheezing and breathlessness. Furthermore it is probable that the fully developed condition can rarely be attributed to a single cause. While infection has usually initiated the process, a number of environmental factors have often contributed to the final state, some of which are occupational and will be considered in this paper. Oswald (1953) maintains that all cases of chronic bronchitis start with infection; this may be true, though it is doubtful if it can be proved, but whether or not a chronic condition develops may well depend on the subsequent treatment of

(*Received for publication September* 9, 1957.)

the respiratory mucous membrane. There is evidence to support the view that there is a complete range of action by occupational factors extending from an almost negligible aggravation to the severe action of aggressive dusts which may be able to initiate bronchitic changes in the absence of infection.

Acute Conditions

The production of an acute bronchitis by irritant gases is well recognised. There is no evidence to suggest that an isolated incident of this nature leads to chronic changes. It is common knowledge that if a healthy man survives the initial gassing he eventually recovers—quickly or slowly according to the nature of the irritant. For instance, following a gassing by chlorine a previously healthy man is usually well inside a fortnight, whereas the effects of gassing by phosphorus oxychloride may persist for several months but eventually disappear. The position is not quite so simple when the patient was already suffering from chronic bronchitis. Here, an acute gassing might be compared with an acute respiratory infection in a chronic bronchitic; such a patient becomes more ill, his illness lasts longer and he may never return to his pre-accident state.

There is another important group of substances which produce acute respiratory distress but which appear to act not as primary irritants but as sensitisers. Certain platinum compounds have long been known to produce an asthmatic response and certain of the chemicals recently introduced into industry produce similar results. I have seen severe asthma produced by one of the di-isocyanates, and similar effects have been reported in workmen exposed to the salts of diazotised aromatic amines. Moore (1956) has reported asthma and bronchitis among men exposed to the inhalation of crude sodium sulphathiazole, and Murray, Fordyce and Lane (1957) have recently reported a peculiar outbreak of purulent bronchitis with bronchospasm among weavers sensitised to tamarind seed size. Doubtless many more instances will come to light as industrial processes change. Provided these acute conditions are recognised early and steps are taken to remove the patient from repeated exposure there is probably little danger of permanent damage. On the other hand, where a man perseveres at his work he may become permanently affected and develop a chronic asthmatic condition in which he readily develops bronchospasm from a variety of trivial causes. This situation can be avoided if the nature and cause of the condition are recognised early and adequate steps are taken to prevent further exposure. This may mean suspension of sensitive individuals from work involving contact with the substance in question until such time as adequate chemical engineering renders the process safe.

Chronic Bronchitis

There are other unpleasant working conditions which produce no violent reaction and are endured year after year without complaint. There has been much conjecture as to the part these might play in injuring the respiratory

tract, but until recently there has been little solid evidence to support such ideas. The difficulty of collecting valid evidence on this subject has already been mentioned. There is probably no disease in which there is a greater chance of multiple causes contributing to the final picture than chronic bronchitis. On the non-occupational side infection, atmospheric pollution, overcrowding, urbanisation and malnutrition have been blamed, while among the occupational factors mentioned are dust, fume, changes of temperature and exposure. In such a situation it is difficult to be certain of the weight to be attached to any particular factor when dealing with an individual patient. Pemberton (1953) has pointed out that this disease is more common in industrial communities " and that there are conditions in our industrial towns and cities which would favour their development," and elsewhere we have shown (Goodman, Lane and Rampling, 1953) the relationship between this disease and a large group of socio-economic factors.

Dust

Pemberton (1953) investigated Sheffield steel workers and found that furnace dismantlers and fettlers of castings who are exposed to high dust concentrations had a specially high incidence of bronchitis and bronchopneumonia even before any suggestion of silicosis had developed. Later, working in America, he (1956) showed a much higher prevalence of chronic bronchitis, emphysema and bronchospasm among coal miners than among two control groups, a finding which he attributed to dust in the mines. He found no correlation between radiological pneumoconiosis and chronic bronchitis and he maintains that the signs and symptoms of chronic respiratory disease in coal workers are usually due to chronic bronchitis and its complications—emphysema and bronchospasm. In a small but careful investigation among gas workers Gregory (1955) found a correlation between the incidence of bronchitis and the number of years worked in a dusty atmosphere. Higgins *et al.* (1956) in a study of respiratory symptoms and pulmonary disability in an industrial town found that miners and ex-miners had significantly more " chronic bronchitis " and a lower ventilatory capacity than men who had never worked in the mine. They also recorded a higher prevalence of respiratory symptoms. Miners without pneumoconiosis were on the average more disabled than those with early simple pneumoconiosis. They were unable to demonstrate any obvious relationship between the length of exposure to dust and bronchitis. The occurrence of respiratory disability among miners has been noted in South Africa, and since 1952 " pulmonary disability " has been accorded official recognition as a disease ranking for compensation in miners, and bronchitis is one of the major factors admitted as a cause of such disability.

The nature of the dust is a matter of importance. Some dusts appear to be able to produce chronic bronchitis much more readily than others. Over forty years ago, for instance, Collis (1915) drew attention to the fact that siliceous dusts were capable of producing chronic bronchitis as well as silicosis and

tuberculosis, while Pemberton (1953) has recently made a similar observation. Certain vegetable dusts have also been shown to produce chronic respiratory disease which in its final form is indistinguishable from chronic bronchitis and emphysema (Schilling, 1956). This capacity of a dust to cause damage to the respiratory tract appears to depend on its physical and chemical properties. Particle size and concentration of the dust cloud are important factors. While there are probably only a few dusts capable of producing bronchitis if breathed in comparatively mild concentrations, most dusts are capable of aggravating an existing bronchitis. It is probable that many apparently inert dusts if inhaled over long periods in sufficiently intense concentrations can produce bronchitis. Some dusts do not appear to produce any damage at all and seem to be satisfactorily eliminated from the lungs. For instance, I was able to examine a small group of men exposed over many years to massive concentrations of pure limestone. Radiographs of these men were completely normal and, what is more striking, these workers showed no history or clinical evidence of bronchitis. It is true they had lived in a rural area, but the excellency of their clinical condition was most impressive (Davies and Nagelschmidt, 1956). This fact regarding limestone was recorded by Collis (1915) over forty years ago; he also found the same freedom from bronchitis among workers exposed to calcium sulphate.

Dusty conditions are likely to be particularly trying and perhaps harmful following acute respiratory infections. There is a clinical impression that an early return to heavy physical work in dusty conditions following an acute respiratory illness may lead to permanent damage to the respiratory system; but at present there is no evidence to support this. Hughes (1957), working from this department, carried out an interesting investigation involving some 750 workers engaged in electricity power stations in the north-west. He was able to compare groups of men working under dusty and non-dusty conditions. He found that there was no difference in the incidence of chronic bronchitis in the two groups, though there was evidence to suggest that those who were " chesty " had been transferred to non-dusty work. He found a marked difference in the absence caused by bronchitis in the two groups both in the number of attacks per man and the length of the attack. In round figures he found that when a " healthy " man with no previous dust exposure had an attack of bronchitis he could be expected to be away from work for two weeks if he were working on a non-dusty job, and for three weeks if he were engaged on dusty work. If such a " healthy " man working on a dusty process had previously worked on a dusty job for more than five years an attack of bronchitis would cause an absence of four weeks and a man known to be " chesty " would be away for five weeks.

Other Factors

While dust is the major occupational factor affecting the bronchitic, several others have been mentioned by various workers; but the evidence is inconclusive and often conflicting. Vernon (1939) suggested that workers exposed to high temperatures suffered an excessive mortality rate from respiratory

disease. Gregory (1955) was unable to confirm either an excessive incidence of, or morbidity from, bronchitis in groups so exposed. Oswald and his co-workers (1953) drew attention to the effects of change of temperature. While it is true that in these patients with an irritable respiratory tract changes of temperature start a fit of coughing, no evidence is available that such working conditions can initiate a chronic bronchitis. It has also been claimed that exposure to the elements may lead to respiratory trouble. The evidence of the Registrar-General would throw some doubt on this, for the standardised mortality ratio for agricultural workers is only 52 compared with 118 for all others in the same social class. But Reid (1957) in a study of London postmen found that a fall in temperature in the presence of sulphur dioxide pollution caused more frequent absence from bronchitis. He concludes that the bronchitis is due to pollution which, of course, the agricultural worker is usually spared.

Job Placement

Since chronic bronchitis is a disease of middle-aged men, the physician is commonly faced with problems created by the need for a change of job. From what has been said ideal working conditions for a patient with chronic bronchitis can be set out. His work should be indoors at an even temperature. The job should be free from dust and fume and should not make excessive physical demands, and his journey to work should not be difficult. Some patients, particularly those with a large degree of bronchospasm, often ask for work in the open air. Unless this is available in a rural area they should be dissuaded from such work. The atmospheric conditions of our industrial towns, particularly during the winter, are considerably worse than those to be found inside factories. Experience shows that provided they are away from dust many chronic bronchitics are happier in the warmth of the coal pit or in the heat of a cotton mill than when they attempt to work in the " fresh air."

" Compensation "

While there is no difficulty in providing Industrial Injury Benefit for the acute cases of bronchitis caused by an accident at work, the same does not apply to chronic bronchitis. It is perhaps not surprising that the provisions of the National Insurance (Industrial Injuries) Act as they apply to this disease have been regarded by some as being unnecessarily rigid. This may have been one of the reasons why a committee was set up in 1953 to review the present provisions of the Act. This committee, under the chairmanship of Mr. F. W. Beney, Q.C., heard a great deal of evidence and reported in 1955 (Cmd. 9548).

Benefit can be paid for an industrial disease only if it is " prescribed." In order to qualify for prescription a disease must not only be shown to be related to occupation, but it must be feasible to prove the causation of the disease in an individual case. Thus, it is not enough to show an excessive incidence of chronic bronchitis in " men exposed to dust." It would also be necessary to be able to incriminate dust as the cause for a particular patient's bronchitis.

While it is probable that prescription of chronic bronchitis might be granted for a clearly defined group of workers exposed to a specific dust if it were shown that these men suffered an exceptionally high incidence of the disease, there is at present no such disease (unless byssinosis is regarded as falling within this category). It would seem, therefore, that so long as the law requires, as a condition of prescription, that the disease in an individual patient can be attributed with reasonable certainty to an occupational factor, it is not likely that chronic bronchitis will qualify for prescription except for very special working groups.

It might be held that the system of prescription should be dispensed with. The Beney committee considered this possibility and alternative systems which might replace it. One of these would be to treat an industrial disease in the same way as an industrial accident. They point out, however, that in the present state of medical knowledge this would be an unworkable method, since it would require individual doctors to answer questions the medical profession as a whole was incapable of answering.

> "A man working out of doors may claim that ordinary climatic conditions were the cause of his arthritis; a clerk may allege that the sedentary nature of his work over many years was responsible for his chronic indigestion, or even his coronary thrombosis; a manager or someone else whose work involves mental stress would claim that this was the cause of his peptic ulcer or perhaps of his neurosis."

Inevitably different decisions would be given in cases presenting identical facts, and claims would be settled on unverifiable opinions expressed by an individual physician. The same situation would arise in many cases of chronic bronchitis, for it will be readily admitted that most cases of chronic bronchitis are not caused by occupation and the extent of any aggravation caused by working conditions cannot be assessed with any accuracy. If the present law is to remain and if the patient with chronic bronchitis is to receive Industrial Injury Benefit, it will be necessary to identify with some precision definite groups of workers where hazards of chronic bronchitis exist and where the disease is so much in excess of normal that prescription is justified. In these circumstances patients suffering from chronic bronchitis who fulfil the necessary requirements regarding their employment would be given the "presumption" that their disease was due to their work. It may well be that the simplest change would be to do away with all extra benefit for industrial accidents and occupational disease and to pay the same benefit to all cases of sickness. Many of the arguments against this simple solution are rooted in the past and perhaps a further examination of the insurance problems along these lines will one day be made.

Prevention

More important than "compensation" is prevention. The problem is difficult and requires for its solution those with various professional skills. There is an important medical question—namely that of identifying with accuracy

and speed the nature of the disease and its occupational cause. Considerable assistance is to be obtained from statistics issued by the Registrar-General. The most up-to-date figures available at present are to be found in the occupational mortality tables based on the 1931 census (Registrar-General, 1938), and in a preliminary analysis of a 1 per cent. sample of the population based on deaths in 1950 and occupations given in the 1951 census (Registrar-General, 1954). For instance, the high mortality rate from chest and heart conditions found among card-room workers led Schilling and others (1952) to investigate this group of workers in great detail and eventually led to an accurate knowledge of the incidence of byssinosis in the cotton industry. It must be emphasised that, in the final analysis, the only way an occupational chest hazard can be established is by painstaking clinical examination of carefully defined populations, including statistically sound controls. Side by side with the examination of people must go an objective assessment of the working environment. Clinical and environmental studies of this kind planned on sound epidemiological lines are costly and time-consuming and the efforts of those capable of carrying them out should be directed to the fields most likely to be fruitful. Fletcher (1956) has recently discussed this problem and has indicated lines among which such enquiries should be made.

When these biological facts have been obtained action lies with others—engineers, chemists and physicists—though the extent and success of their efforts may depend on economics and will be determined by administrators and industrialists. It will sometimes be difficult to secure action even when the facts are established and it may be necessary to secure the support of the law. Already our legislation goes some way in this matter and doubtless as knowledge grows this will be modified accordingly. The lead, as always in matters of this sort, must be given by enlightened employers and already there is evidence that this is being given by sections of nationalised and private industry.

Summary

Over and above the acute respiratory conditions produced in industry by irritant and sensitising substances it is probable that long-term changes which give rise to the symptom complex of chronic bronchitis can be caused or aggravated by the working environment. There is evidence that prolonged exposure to dust can cause harm to the respiratory tract and that certain dusts are more capable of producing damage than others. In most cases there are non-occupational factors which contribute to the final condition, with the result that it is impossible to be sure of the part occupation has played in any particular patient, and in consequence the disease does not qualify for prescription under the Industrial Injuries Act. There is need for further field investigations aimed at identifying with precision the occupational hazards likely to lead to chronic bronchitis. This would not only enable " compensation " to be granted in appropriate cases but, what is more important, it would make it possible to institute preventive measures.

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ON ACTION OF 5-BROMOSALICYLHYDROXAMIC ACID AGAINST DRUG RESISTANCE IN TUBERCULOSIS

By S. Hornung, *of the Institute of Tuberculosis, Warsaw, and Medical Academy, Cracow;* F. Amałowicz, *Sanatorium in Wysoka Łąka;* Z. Broda, *Sanatorium in Górno;* Z. Neciuk-Szczerbiński, *Sanatorium in Wysoka Łąka;* E. Paryski, *Chałubiński Sanatorium in Zakopane;* M. Polończyk, *Medical Academy, Cracow;* and T. Rapf, *Medical Academy, Cracow*

It is well known that isonicotinic acid hydrazide (INAH), loses its therapeutic properties after being administered for some time and that INAH resistance generally develops within the first three months (Omodei Zorini, 1953; Lotte, 1953; Bernard, 1954; Fox, 1955; and others).

It is also known that the most efficient method of counteracting this phenomenon is the simultaneous administration of another, possibly less potent, antituberculous agent such as p-aminosalicylic acid (PAS.) Often, however, the administration of PAS or its derivatives must be interrupted or even abandoned because of its irritating action on the mucous membranes of the gastro-intestinal tract, especially if given by mouth.

The present paper deals with clinical experiments on using 5-bromosalicylhydroxamic acid (called " T40 ") in combination with INAH.

Salicylhydroxamic acid and, later, 5-bromosalicylhydroxamic acid were suggested by T. Urbanski (1949-52) as antituberculous agents. Ślopek (1953) found it effective in experimental tuberculosis in mice when a chronic form of the disease was developed, although it was ineffective in acute experimental tuberculosis.

5-Bromosalicylhydroxamic acid has been found of low toxicity (Venulet, 1953; McIsaac and Williams, 1955-56) and given clinical trial. It has been well tolerated by patients in daily doses of 3-4 g., given by mouth, and some interesting results have followed (Hornung *et al.*, 1953). It was felt that it might be as efficient as PAS if given in combination with INAH and the results of the experiments *in vitro,* by Buraczewska and Manowska (1955), proved this contention. Hornung, Polończyk and Rapf (1956) investigated the problem clinically. The results of these experiments, limited though they were, supported the combination of INAH and T40 for therapeutic use.

In the Tuberculosis Institute in Prague, Křivinka and Styblo (1956) investigated INAH resistance in 30 patients treated with INAH and T40 for 110 days. One case developed a moderate resistance (up to 10 mcg./ml.). Resistance to lower concentrations of the drug (*e.g.* 1 and 5 mcg./ml.) is not reported.

In this paper we describe an investigation of the effect of T40 on the

(*Received for publication July* 15, 1957.)

resistance to INAH in the combined INAH+T40 treatment. The study was planned as a team by the Committee on Chemotherapy of the Research Council of the Tuberculosis Institute, who enlisted fifteen heads of various Health Services (University Clinics, Sanatoria and Hospital Divisions). Bacteriological and resistance studies of the cultured strains were to be carried out in six laboratories. One of us (Hornung) was charged with co-ordinating the work. Methods for testing the INAH resistance of tubercle bacilli were explained in detail by Buraczewska.

At the end of 1956 the work was completed according to plan, in four institutions, by the authors of the present report. In addition, Pręgowski, Gofron and Broda published their results from the sanatorium in Bystra, Silesia, and this data was included if it fitted strictly into the problems under discussion.

Our aim was to compare the INAH resistance in two series of patients, one of which was given INAH and T40 for three months, the other one INAH and PAS for an equal length of time. The results from both series were finally to be compared with the results published by other authors in relation to patients treated with INAH alone.

The total number of our patients was 167. Table I shows the development of the resistance of strains of *Mycobacterium tuberculosis* before and after a three months' course of treatment with INAH and T40.

TABLE I.—SENSITIVITY AND RESISTANCE OF *Mycobacterium tuberculosis* TOWARDS INAH
Patients treated with INAH+T40

Before the treatment			*After three months of treatment with INAH+T40*									
			Sensitive		*Resistant at concentrations of INAH*							
					0·5 mcg./ml.		5 mcg./ml.		10 mcg./ml.		25 mcg./ml.	
Degree of sensitivity and resistance towards INAH	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%
Full sensitivity	75	100	40	53·3	14	18·7	3	4·0	8	10·7	10	13·3
Resistance at concentrations												
0·5 mcg./ml.	15	100	8	53·3	2	17·8	1	6·7	4	26·6	—	—
5 mcg./ml. ..	4	100	1	25·0	1	25·0	1	25·0	1	25·0	—	—
10 mcg./ml. ..	7	100	6	85·7	—	—	—	—	—	—	1	14·3
25 mcg./ml. ..	18	100	2	11·0	1	5·5	1	5·5	3	16·7	11	61·1
Total ..	119	100	57	47·8	18	15·1	6	5·4	16	13·4	22	18·4

In our series there were 75 patients from whom we obtained a culture of *Mycobacterium tuberculosis* fully sensitive to INAH—*i.e.*, showing growth inhibition even at the concentration of 0·5 mcg./ml. INAH. Some of these patients had been treated previously with INAH. We also analysed the development of the resistance in the cases which could be called occult. Six

patients in this group gave a history of having taken over 1,000 tablets of INAH—*i.e.*, over 50 g. of the drug—before being included in our series. They received it in some instances combined with other drugs, but more often as the only form of chemotherapy. Only one of these six patients kept his full sensitivity after the three months of planned treatment (INAH+T40). (These patients were sensitive to 10-25 mcg./ml. INAH, 1-5 mcg./ml. and 1-0·5 mcg./ml.).

This observation is based on a small number of cases, but it suggests that at the beginning of our investigation—*i.e.*, before the three months' course of administration of INAH+T40—there was already a sub-threshold occult resistance to the drug in the patient, who had previously been given a large global dose of INAH. The addition of another agent could not prevent its

TABLE II.—SENSITIVITY AND RESISTANCE OF *Mycobacterium tuberculosis* TOWARDS INAH WITH EXCLUSION OF SIX PATIENTS WHO TOOK 50 G. OF INAH PRIOR TO THE TREATMENT

Before treatment		*After three months of treatment with INAH+T40*									
Full sensitivity		*Sensitive*		*Resistant at concentrations of INAH*							
				0·5 *msg./ml.*		5 *mcg./ml.*		10 *mcg./ml.*		25 *mcg./ml.*	
Number of cases	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%
69	100	39	56·5	13	18·8	2	2·9	7	10·2	8	11·5

TABLE III.—SENSITIVITY AND RESISTANCE OF *Mycobacterium tuberculosis* TOWARDS INAH
Patients treated with INAH+PAS

Before the treatment			*After three months of treatment with INAH+PAS*								
			Sensitive		*Resistant at concentration of INAH*						
					0·5 *mcg./ml.*		5 *mcg./ml.*		10 *mcg./ml.*		25 *mcg./ml.*	
Degree of sensitivity and resistance towards INAH	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%
Full sensitivity	24	100	14	58·3	3	12·5	2	8·3	5	20·8	—	—
Resistance at a concentration												
0·5 mcg./ml.	8	100	2	25·0	3	37·5	—	—	2	25·0	1	12·5
5 mcg./ml. ..	5	100	1	20·0	—	—	2	40·0	2	40·0	—	—
10 mcg./ml. ..	6	100	2	33·3	—	—	—	—	3	50·0	1	16·7
25 mcg./ml. ..	5	100	1	20·0	—	—	1	20·0	1	20·0	2	40·0
Total ..	48	100	20	41·6	6	12·5	5	10·4	13	27·0	4	8·3

distinct appearance. The difference in behaviour in this group of patients justifies the exclusion of the whole series of six cases, initially fully sensitive to INAH, in order to obtain a more accurate picture. After this correction the group of fully sensitive cases presents a slightly different picture (Table II.)

Simultaneously with the serial studies of the effect of T40 on the INAH resistance, similar investigations were carried out with PAS, by the method now commonly accepted.

The results of the investigation of resistance in this group are shown in Table III.

The figures included in Table III as compared with those in Table I show no significant differences.

In this situation the most interesting problem would be to compare the results obtained from our own material treated with combined therapy, with similar results from tuberculous patients treated with INAH alone. Numerous authors in many countries stated unanimously that the resistance to INAH develops rapidly. We give for example the figures of the Medical Research Council (Report 4), Table IV.

TABLE IV.—SENSITIVITY AND RESISTANCE OF *Mycobacterium tuberculosis* TOWARDS INAH
Patients treated with INAH alone—according to Medical Research Council Report 4

Before the treatment		*After three months of treatment with INAH+T40*											
Sensitive		*Sensitive*		*Resistant at concentrations of INAH*									
				0·2 *mcg./ml.*		1 *mcg./ml.*		5 *mcg./ml.*		10 *mcg./ml.*		50 *mcg./ml.*	
Number of cases	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%	*Number of cases*	%
132	100	27	20·4	20	15·2	22	16·6	10	7·6	13	9·8	40	30·4

The plan of our investigation involved the study of two groups of patients—one of which was going to receive 0·3 g. INAH and 3 g. T40 *per os* daily, and the other one the same amount of INAH and 10 g. of PAS daily. Before beginning this course of treatment a culture of *Mycobacterium tuberculosis* on a solid medium had to be obtained in each case and its sensitivity to INAH determined, and the same procedure was necessary after the completion of the three months' course of treatment. It was to be expected that a considerable number of patients included in the experiment would have to be excluded before the conclusion of the investigation, because, following the treatment and consequent improvement in their condition, the bacilli would have disappeared from their sputum.

The instruction for determining the INAH resistance recommended the use of subcultures, inoculated within a week of the emergence of growth on the initial culture. It was decided that the investigation should be carried

out on egg glycerine solid media of Loewenstein and Jensen. The following medium concentration of INAH were used: O=control; 0·5; 5; 10 and 25 mcg./ml. One week after the beginning of growth on the control medium without INAH content, the state of growth of the *Mycobacterium tuberculosis* was read in the remaining test tubes containing media with the above-mentioned INAH concentrations.

The results of our investigation on a series which allowed the drawing of definite conclusions were subjected to statistical analysis, and they proved that in clinical use T40 definitely counteracts the rapid emergence of INAH resistance. This effect is approximately equal to the effect of PAS. Considering the large doses of PAS required for obtaining an effect and the fact that it is so badly tolerated on the one hand, and the smaller amounts of T40, which is so well tolerated, although also given by mouth, on the other, the superiority of 5-bromosalicylihydroxamid acid is obvious.

From the above it seems logical to conclude that the use of T40 should be introduced into the routine treatment of tuberculosis in cases where INAH is indicated, to replace the more expensive and less well tolerated PAS.

We analysed statistically the results obtained, using the formulæ for the statistical significance of difference and the x^2 test.

We compared the group of patients treated with INAH+T40 (Table III) with the group of those treated with INAH alone (Table IV). We took for comparison these patients from both groups in whom before the beginning of the treatment tubercle bacilli were sensitive to INAH; the number of patients in the group INAH+T40—75 patients treated with INAH+T40 for three months (Table I) with the group of 24 patients treated with INAH+PAS for the same length of time (Table III)—showed that in the first group (INAH+T40) the tubercle bacilli were fully sensitive to INAH in 40 cases (53·3 per cent.) and in the other group (INAH+PAS) they were fully sensitive in 14 cases (58·3 per cent.); this difference is not statistically significant (t=0·43). The number of cases in which there appeared strains resistant to INAH in concentrations of 5-25 mcg./ml. after three months of treatment was 21 (28 per cent.) in the INAH+T40 group and 7 (29 per cent.) in the group INAH+PAS, which is also statistically insignificant (t=0·10).

By applying the x^2 test to all the values of both columns we obtain x^2=6·15, which corresponds to $P<0·2$ and shows that there is no statistical difference. The statistical test proves, therefore, that there is no difference in the incidence of INAH resistance between the cases in which INAH is given with PAS or with T40.

We then compared the group of 75 patients treated during three months with INAH+T40 (Table I) with a group of 132 patients from the Medical Research Council, treated for an equal length of time with INAH alone (Table IV). In this group of 132 patients treated for three months with INAH alone there were 27 cases (20·4 per cent.) in which the tubercle bacilli remained fully sensitive to INAH. This figure compared with the group of 40 cases (53·3 per cent.) treated with INAH+T40 shows a highly significant difference (t=4·75).

The number of cases in which after three months of treatment there emerged tubercle bacilli resistant to concentrations of INAH of 5-25 mcg./ml. was in the INAH+T40 group 21 (28 per cent.) and in the group of INAH alone—63 (47·8 per cent.), which constitutes a significant statistical difference ($t=2·92$).

The x^2 test if applied to all the values of both columns gave $x^2=82·06$, corresponding to $P<0·00001$, which proves a highly significant difference between the behaviour of the INAH resistance in the group INAH+T40 as compared with the group treated with INAH alone.

Summary

Two groups of patients have been treated with isonicotinic acid hydrazide (INAH) with 5-bromosalicylhydroxamic acid (T40) or *p*-aminosalicylic acid (PAS) for three months.

One group of 119 was treated with INAH+T40, a second group of 48 was given INAH+PAS.

Resistance of mycobacteria Tb towards INAH has been followed in the course of treatment.

Before treatment 75 patients in the group INAH+T40 and 24 patients in the group INAH+PAS showed a full sensitivity of bacteria towards INAH.

After treatment, in 40 cases (53·3 per cent.) out of 75 patients of the first group and in 14 cases (58·3 per cent.) out of 24 of the second group bacteria remain sensitive towards INAH.

Both figures are essentially the same ($t=0·43$).

The number of cases where strains of bacteria developed resistance towards INAH (at concentration 5-25 mcg./ml.) were:

in the group INAH+T40	.. ..	21 (28 per cent.)
and in the group INAH+PAS	.. ..	7 (29 per cent.)

Both figures are essentially the same ($t=0·10$).

Comparison of the group of 75 patients treated with INAH+T40 with the group of 132 treated with INAH alone, according to the statistics by the Medical Research Council (Report 4), gives results clearly in favour of treatment with INAH+T40. In the case of treatment with INAH alone only 27 patients (20·4 per cent) remained with bacteria sensitive towards INAH. With INAH+T40 the figure was 53·3 per cent. This gives a high difference ($t=4·75$), $x^2=82·06$ and $P<0·00001$.

Addition of T40, which is well tolerated by patients, should be introduced into the routine method of treating tuberculosis with INAH.

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SURGERY OF ŒSOPHAGEAL LESIONS

By T. Holmes Sellors

From the Middlesex and London Chest Hospitals

Many individuals go through life practically unaware of the fact that they possess an œsophagus, but those who are afflicted with a lesion of the gullet are painfully conscious of any abnormality in swallowing. The inability to swallow food normally as the result of an obstruction is quickly recognised, but the discomforts of œsophagitis, acid reflux from the stomach or localised spasm are very real and often severe. A chronic œsophageal lesion often produces symptoms whose existence is only realised after the disorder has been corrected. Patients become acclimatised to discomfort over a period of months or years and only realise the benefits of normality after treatment. Most patients can accurately locate the actual site of a lesion by pointing over the sternum, but a common complaint, even for a low œsophageal abnormality, is a sensation of "hold up" and discomfort at the upper end. Conditions that have led to adhesion of the œsophagus within the mediastinum give a sense of oppression or pain in the back.

Until recent years œsophageal surgery has been of limited scope. Œsophagotomy or œsophageal resection was too often followed by a leak or fistula which produced pleural infection with lethal results. The absence of a serous coat to the œsophagus was thought to be the deterrent factor to healing, but in the last decade it has been shown that the œsophagus will heal or unite. This is largely due to technical improvements, the use of antibiotics and early and complete re-expansion of the lung after operation. In this country it was Vernon Thompson who first restored continuity of the œsophagus after removal of a malignant growth. Prior to this, exteriorisation of the œsophagus or gastrostomy was the only way in which a patient's life could be prolonged in the face of œsophageal obstruction. Many attempts at reconstruction were made in the early days of œsophageal surgery using skin-flap tubes and the like, but these have now been replaced by anastomosis of the œsophagus within the mediastinum to stomach or small bowel.

Endoscopy has played a large part in the diagnosis and treatment of conditions such as strictures and retained foreign bodies, and any surgeon practising surgery of the œsophagus must be conversant with this technique and at the same time realise its benefits and limitations. It is not an easy procedure to master.

A complete discussion on œsophageal disease is beyond the compass of a short article and comments will only be made on the current practice in some of the more important conditions, taken in the order of the ages at which they appear.

(*Received for publication September* 23, 1957.)

Congenital Atresia

Congenital atresia of the œsophagus takes a variety of forms and may be associated with other visceral lesions for which no treatment may be possible. There are, however, a group of cases in which the obstruction occurs at the level of the tracheal bifurcation. Below this a normal œsophagus may exist and there is frequently a communication with air passages. If the condition is recognised before the baby has flooded the lungs with food and secretions surgery is indicated. The diagnosis is established by radiography—no gas is present in the abdomen and the instillation of 1 or 2 ml. of lipiodol into the gullet will demonstrate the obstruction. The fluid balance has to be carefully established and all food is withheld.

The operation consists in a transpleural or extra-pleural thoracotomy on the right side. The azygos vein is divided and the dilated upper segment of the œsophagus is freed and detached from the trachea. A fine catheter is passed through this upper segment and into the lumen of the collapsed lower œsophagus after ensuring that there is an adequate blood supply to the lower segment. Fine interrupted sutures, sometimes under considerable tension, are used to join the ends together and the chest is closed with suction drainage.

There is nothing to lose from operating—untreated obstruction means a dead baby. Not every attempt is successful, but the increasing proportion of those that survive at the present time is a tribute to medical progress. The co-operation of surgeon and pædiatrician has paved the way in giving these infants a chance of survival. The names of Cameron Haight, Swenson and Belsey stand out as pioneers in this branch.

Strictures

The swallowing of corrosive fluids such as petrol, paraffin and other agents can lead to the most devastating form of stricture in the œsophagus. Many of these obstructions occur in children who accidentally or unwittingly drink the substance. In older people attempted suicide is a frequent cause of this lesion. The stricture is generally long and as soon as dysphagia starts it is important to try to preserve or dilate the cicatrising area with bougies. Repeated and often tedious œsophagoscopies and dilatations may manage to preserve a sufficiently wide channel for the swallowing of fluids, but on occasions gastrostomy will be required to prevent starvation. Major surgery is the last resort in children, but if dilatation fails the only solution is to mobilise the stomach or a section of the jejunum and bring it into the mediastinum for anastomosis with normal œsophagus above the stricture.

Foreign Bodies

Impacted foreign bodies in the gullet require early removal before their sharp edges ulcerate into the mucosa and lead to the risk of perforation. Simple measures such as the swallowing of soft bulky material will invariably have been tried as a preliminary, but if the evidence of impaction remains œsophagoscopy

is indicated. The work of Chevalier Jackson and others gives evidence of the remarkable ingenuity and success that can be achieved in the recovery of bizarre-shaped objects, notably safety-pins and the like which are particularly liable to cause perforation. Unfortunately a formal attempt at removal is often delayed until there is considerable local inflammation with œdema and granulation of tissue which complicate the task. In these cases instrumentation may easily lead to perforation and a decision has to be made as to whether direct œsophagotomy would be safer. Exposure of the œsophagus through the open chest is not difficult and the object can be removed with the minimum of further trauma and the œsophagus closed by careful suture. There is no place for a retrograde approach to the œsophagus through the stomach as was formerly advocated.

Achalasia

Achalasia of the cardia or cardiospasm is a condition which has a marked psychosomatic ætiology. The cause is unknown, but the condition starts in early adult life and is usually tolerated for a number of years before the necessity for treatment is obvious. The œsophagus dilates to an enormous size and ultimately is converted into a non-elastic bag or sac with convolutions whose outlines are visible radiologically. The failure of the œsophagus to empty readily leads, sooner or later, to " spill over " into the lungs and the formation of a chronic lipoid type of pneumonia that is often mistaken for tuberculosis.

In the early stages cardiospasm responds to antispasmodic drugs, notably octyl nitrite, and expiratory breathing exercises, but a more successful treatment is to dilate the " cardia " forcibly with a hydrostatic dilator. A Negus bag is the most satisfactory instrument and a number of cases are cured by one or more dilatations. The regular passage of bougies by the patient (Hurst's mercury bougie) has little to recommend it now that other methods are available.

The failure of forcible dilatation brings surgical treatment into the picture. Operation should not be postponed unduly if symptoms persist, and of the many operations that were originally described the only procedure that need be considered is Heller's operation. In this the longitudinal coats of the œsophagus are divided and the mucosa is allowed to bulge through the incision from the upper part of the stomach for 3-4 inches into the œsophagus in the manner of Rammstedt's operation on the pylorus. The interesting point in this operation is that few circular œsophageal fibres are encountered and that there is no evidence of a cardiac sphincter as has been described in anatomy textbooks. The so-called cardiac sphincter is a functional one produced by the diaphragmatic ring fibres on the œsophagus. Neither is there any intra-abdominal œsophagus.

Heller's operation, though frequently performed through the abdomen, is more easily carried out through the left chest, where a full exposure of the affected area is obtained. The result of the operation is dramatic and the patient immediately states that he or she can swallow normally. If the œsophageal dilatation above the stricture is not excessive the symptoms are

usually completely relieved, and as the anatomical relations of the œsophago-gastric region have not been disturbed regurgitation or reflux of gastric contents does not occur. Recurrence of symptoms after a number of years has occasionally been recorded but the operation can be repeated on the opposite side.

Ruptures

Sudden bursting of the lower œsophagus is being recognised with increasing frequency. Over-eating and excessive alcohol appear to be contributory factors and the catastrophe overtakes the patient with the same dramatic effect as a perforated peptic ulcer. The presence of fluid and gas in the chest suggests the diagnosis, which calls for immediate thoracotomy. The tear in the œsophagus is readily recognised, and after the ingested food and drink have been removed from the pleural cavity the œsophagus is repaired carefully in layers and the chest closed with suction drainage. The risk of an empyema and an œsophageal fistula is very real. If the lung can be fully expanded it will become adherent to the suture line in the œsophagus and act as a barrier against later leakage. Repair of an œsophageal tear that is several days old is almost impossible because of the friability of the tissues, and in some cases the only solution lies in resection and anastomosis of healthy œsophagus to mobilised stomach.

Hiatus Hernia

The work of Allison and Barrett has done much to clarify the anatomy of the œsophageal hiatus and hernia formation and it is now possible to have a more precise understanding of this form of herniation.

There are a number of antagonistic forces working to hold the lower œsophagus and upper stomach in place. The powerful longitudinal fibres of the œsophagus and the sub-atmospheric pressure within the thorax exercise powerful retraction upwards. This is resisted by the stomach, or body of the bottle, with its neck which is held against the V-shaped opening of the diaphragmatic ring fibres, and by the ligamentous attachments of the stomach. The " cardia," or neck of the bottle, lies in the diaphragmatic hiatus which is formed by a powerful loop of muscle fibres arising from the *right* crus and strengthened by fibres from the left crus. These crural fibres resemble the flaps of a coat which overlap on being buttoned up and narrow the neck opening. Constriction of these fibres on inspiration pulls the œsophagus backwards towards the vertebral column and hinders the passage of food or liquid appreciably. The other significant factor is the non-return action of the œsophago-gastric junction. This is primarily effected by the angle at which the gullet enters the stomach: the big gas bubble in the fundus keeps the stomach high and well up under the left dome of the diaphragm so that reflux is prevented.

Interference with any of these mechanisms can produce a complicated train of events. For example, in a fat middle-aged person who is particularly liable to develop a hiatus hernia there is loss of muscular tone, the abdominal ligaments lose their elasticity and there is considerable increase in abdominal

pressure as the result of fat. The properitoneal fat on the upper surfaces of the stomach close to the hiatus protrudes into the chest, the gastric ligaments cannot hold the stomach in place and the pull of the œsophagus causes the functional " cardia " to rise through the weakened diaphragmatic ring. The angle between œsophagus and stomach is rendered less acute and some reflux of gastric contents is possible. The regurgitation of acid into the lower œsophagus, recognised only too well by the patient as heartburn, produces irritation and spasm which further exaggerate the pull of the longitudinal fibres of the œsophagus. This is the basis of the sliding hernia in which the œsophagus is shortened or at any rate displaced above the ring. It is probable that the para-œsophageal hernia in which the œsophago-gastric junction is in its normal position and a bulge of stomach enters the chest alongside it through the ring does not exist. What does happen is that once the slide has started the ring is large enough to allow stomach (fundus) to pay off through the hiatus and lie against the œsophagus to form an hour-glass appearance, the waist being produced by the constriction through the diaphragm.

The classification of sliding herniæ into two groups explains the symptomatology. The hernia in which the acute angle of entry is lost is liable to reflux of gastric contents with heartburn and regurgitation as the dominant features. If a bulb of stomach lies in the chest the symptoms are those of a gall bladder, fullness after a few mouthfuls of food, flatulence, belching and a sense of fullness that persists until the bulb has emptied. Palpitations and substernal discomfort are readily explained by pressure of the intrathoracic gastric bulb on the stomach and mediastinum. The persistence of œsophagitis will in time lead to fibrosis and stricture formation which produces dysphagia to add to the patient's discomfort. In such cases the shortening of the œsophagus plus the stricture cause considerable difficulties in the surgical repair.

Not all sliding herniæ are permanent and progressive. The heartburn of pregnancy is associated with a small hiatus hernia produced by the increased abdominal pressure and this resolves when the uterus is emptied. With loss of muscle power and elasticity a hernia which has once started will persist, though in the erect posture the stomach may return to the abdomen. It is this mobility that delays the radiological recognition of the condition in many cases.

The incidence of hiatus hernia is far higher than is generally suspected. To date only the more severe cases have been recognised, but with increasing awareness of the condition and the use of the Trendelenburg position in radiological screening of barium meals many cases hitherto labelled under very different diagnoses have come to light. One cannot exclude the association of gall bladder disease, peptic ulceration and so on with hiatus hernia, but it must be recognised that many of the apparently small and insignificant forms of herniation give rise to severe symptoms.

The common sufferer from this disorder is, as has been indicated, the typical gall bladder type—a middle-aged or elderly woman, fat, flabby, flatulent and with some degree of hypertension—an admittedly poor subject for surgery; but as conservative measures have little if anything to offer they are willing to accept the risks of operation. Many, when told that only an operation will

give them any relief, reply immediately that they want it done as soon as possible. This is some indication of the discomfort that they are suffering and cannot adequately put into words. Naturally a wholesale surgical approach to the problem would be unwise. Many patients would be unsuitable and many have to undergo weight reduction as a preliminary, but age in itself is no contra-indication. Patients in the seventies are frequently operated on and are among the most satisfactory results.

What has probably delayed a full surgical approach to the problem has been the uncertainty of the operative results. In early series of cases that were accurately followed up the recurrence rate varied from 10 to 15 per cent., but in the last few years technical improvements have reduced this considerably.

There is a constant dispute as to whether the hernial repair should be done through the abdomen or chest. Thoracic surgeons have no hesitation in advocating the latter approach which gives a better exposure with less discomfort to the patient.

The principal details of repair of a hiatus hernia are, first to free the lower œsophagus and ensure its mobility and to identify the hernia and the diaphragmatic ring. The hernial sac and bulky fatty tissue are excised if they are present. The stomach is then reduced into the abdomen by passing a tape placed round the œsophagus through a small incision in the dome of the diaphragm. A small area of the fundus of the stomach is sutured to this diaphragmatic incision, which is carefully closed. Next, a series of sutures are placed between the lower inch of the œsophagus and the muscle fibres of the ring, and finally the V-shaped gap posterior to the œsophagus formed by the crural fibres is overlapped by two or three stout sutures. In this triple repair the acute angle between stomach and œsophagus is restored, the œsophagus is stitched down at full length and the posterior deficiency is closed.

The symptomatic relief after operation is often remarkable and the patients have to be warned not to put on weight too rapidly, as it may be the first time that they have been able to eat in comfort for years. Associated abdominal disorders, such as ulcer or gall bladder disease, will lead to persistence of symptoms, and if the thoracic route is used particular care has to be taken as a preliminary to exclude lesions of this type. If a recurrence should occur it may be symptomless, but more commonly the patient is again subjected to pain and heartburn which, if severe, may require a further operation.

Carcinoma of the Œsophagus

Though there are two traditional sites for intrathoracic œsophageal cancer, at the level of the bifurcation and at the lower end, a growth can occur in any part of the gullet and its presence is indicated by increasing dysphagia which is accurately localised. The patient is first unable to swallow solids, then semi-solids, and finally liquids fail to pass when the obstruction is complete. The condition should be diagnosed long before starvation occurs, but many patients do not seek advice until too late. In the localisation of the size and extent of the tumour radiology can give considerable help.

Not many years ago gastrostomy was the only method of palliation; it carried a high mortality and did little to improve the patient's lot. The alleged inability of the œsophagus to heal and the risk of mediastinitis precluded major surgery until the pioneer efforts of Grey Turner and others showed that the whole œsophagus could be removed. In this type of operation the upper end was exteriorised in the neck and a gastrostomy was performed after the growth was removed. This procedure did not allow patients to eat or swallow normally and various efforts were made to construct a subcutaneous œsophagus with skin tubes and jejunal loops. Unfortunately many patients died from recurrence during the process of these plastic operations and it was then realised that œsophageal cancer was not the relatively benign slow-growing tumour that it was thought to be. Previously, patients died of starvation before the growth had progressed too far.

Attention was then turned to trying to restore continuity within the chest by mobilising the stomach and bringing it up into the chest. The first attempts were made on tumours at the lower end, where two histological forms are recognised, a squamous-cell type and an adenocarcinoma ascending from the stomach to obstruct the gullet. A left thoraco-abdominal exposure with division of the diaphragm gives an excellent exposure of the lower chest and upper left quadrant of the abdomen. The growth is dissected free and removed with an extensive bloc of the glandular field if possible. Then, according to the area of stomach removed, the stump of stomach, duodenum or jejunum is anastomosed to the œsophagus.

As a result of a successful operation the patient is able to eat and drink in comfort, but in terms of " cure " the results are less satisfactory. Failure to effect complete clearance of the growth or glandular field leads to recurrence in many cases, but with an adequate operation on an early case there is a reasonable proportion of five-year survivals. Increasing the extent of the operation to clear submucous infiltration, which is often well above the macroscopic tumour, appears to be giving better results than formerly. If the growth cannot be removed a short circuit with an œsophago-gastric anastomosis above the obstruction allows the patient to swallow and live in reasonable comfort for six months to a year.

Growths in the middle or upper parts of the œsophagus are more difficult to handle. Mobilisation of the stomach, while preserving the lower vascular arcades, allows the fundus to be brought up as high as the neck without endangering its blood supply. The upper œsophagus can be approached from the left, but it is more straightforward to use a right thoracotomy, since after dividing the azygos vein the whole length of the œsophagus is freely exposed.

The chances of major surgery in these cases are very much influenced by the general condition of the patient, but even if the growth cannot be removed a short circuit may well be worth while. The operation consists in a laparotomy with division of the left gastric artery and vasa brevia plus clearance of omentum to allow full mobility of the stomach. The peritoneum over the œsophageal hiatus is divided and the abdomen closed. The next step is to open the right chest and free practically the whole œsophagus, including the growth. The

stomach is then pulled into the thorax and an anastomosis made well above the arch of the aorta between the œsophagus and the fundus. There is inevitably some tendency to ileus after operation, but the patient encounters little discomfort in swallowing or eating. The only warning to be given is to avoid reflux from the stomach by keeping in an erect or semi-erect posture—not sleeping flat or bending forwards.

If it is not possible to carry out radical or palliative surgery gastrostomy may have to be considered, but attempts should first be made to dilate the obstruction and insert a Souttar's tube which will at any rate permit the swallowing of fluids and semi-solids.

Treatment is clearly far from ideal, but there has been considerable improvement and in many cases prolongation of life has been achieved. Parallel with surgical progress there has been a revival of interest in modern radiotherapeutic measures. In many cases some resolution of the tumour mass can be achieved with improvement in swallowing, but even if considerable resolution occurs there is always the risk of later stricture formation which in itself may constitute a formidable problem. In general it is probable that the results of radiotherapy cannot as yet equal those of surgery, such as they are, but any measure which brings relief is worthy of careful consideration. The diagnosis of cancer of the œsophagus is no longer a death sentence from slow starvation.

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PULMONARY MYCOSES OCCURRING IN BRITAIN

By R. W. Riddell and Yvonne M. Clayton

Bacteriology Department, Brompton Hospital, London

Fungous diseases of the lungs may be divided into those in which infection is acquired endogenously and those of exogenous origin. They are not known to be transmissible from person to person.

Endogenously Acquired Infections

These are caused by organisms which occur frequently as normal inhabitants of the mouth and upper respiratory tract. The organisms to be considered are *Candida albicans*, a yeast-like fungus responsible for moniliasis, and *Actinomyces israeli*, a filamentous bacterium causing actinomycosis.

(1) *Moniliasis*

Candida albicans has not been incriminated with certainty in Britain as a cause of pneumonia and from recent experience there has been little to add to Shrewsbury's (1936) conclusion that the extent of the pulmonary pathology produced by this yeast is "secondary thrush of the bronchi." Other yeast species commonly present in the mouth and upper respiratory tract do not appear to be capable of producing disease. Certain prerequisites appear necessary before *Candida* infection becomes established, such as excessive antibiotic therapy or the existence of some debilitating disease. It should be emphasised that *C. albicans* may be profuse in bronchial exudates in the absence of any evidence of pathology attributable to it.

The variety of yeasts cultured during routine bacteriological examination of sputa is exemplified in Table I. These results deal with 1,060 consecutive

Table I

Yeast isolated	*No. of patients* (1,060 *examined*)	*% of patients*
CANDIDA ALBICANS	425	40
Candida tropicalis	46	4·3
Candida pseudotropicalis	15	
Candida krusei	13	
Candida parakrusei	6	
Candida pelliculosa	3	
Torulopsis glabrata	50	4·7
Unidentified	8	
None	520	

(*Received for publication August* 16, 1957.)

patients receiving treatment at the Brompton Hospital for various conditions and being investigated by culture studies at 37°C.

Candida albicans occurred with much the greatest frequency (40 per cent. of all patients), the next most common being *Torulopsis glabrata* and *Candida tropicalis* (4·7 and 4·3 per cent. of patients respectively); a further 4 per cent. of patients harboured other yeast species. The frequency with which two or more species are recorded as present in sputum samples will largely depend upon the care exercised in colony selection. Forty-five of the 425 patients harbouring *C. albicans* in the above series grew some other fungus as well, usually a yeast.

In Table II the yeast species isolated from sputa of 900 patients are correlated with the main diseases for which treatment was being given.

TABLE II

Disease	*No. of cases*	*Yeasts grown*		
		C. albicans *with or without other yeasts*	*Other yeasts only*	*None*
Bronchitis	274	113 (41%)	32	129
Bronchiectasis	98	33 (34%)	5	60
Asthma	76	29 (38%)	2	45
Asthma+bronchitis	40	17 (43%)	1	22
Pneumonia	70	39 (56%)	7	24
Tuberculosis	90	30 (33%)	7	53
Carcinoma	75	30 (40%)	9	36
Aspergillosis	16	9	2	5
Lung abscess	10	6 (42%)	1	3
Sarcoidosis	7	3	1	3
Other	144	56	20	68
Total	900			

In the above disease groups the proportion of patients harbouring *C. albicans* is approximately the same. This yeast is invariably isolated from patients suffering from oral or bronchial thrush.

Childs (1956) showed that there is a quantitative increase of *C. albicans* in the sputum of patients being treated with certain antibiotics. Responsibility for illness is sometimes ascribed to this fungus when it comes to predominate over the bacterial flora in sputum cultures. This may, perhaps, be justified when clinical deterioration is coincident with increase of *C. albicans* cells in sputum and with disappearance of antibiotic-sensitive bacteria, and, furthermore, when both reduction of *C. albicans* in sputum and clinical improvement follow the termination of antibiotic therapy (Wolff, 1952; Bass *et al.*, 1954). Expectoration of thrush membrane is obviously pathognomonic of disease, but this is of uncommon occurrence (Browne, 1954). Observations made at autopsy are difficult to interpret, for the proliferation of *C. albicans* in diseased bronchial mucosa and other tissues is so immediately obvious histologically

that it is tempting to incriminate the yeast and to absolve from responsibility pathogenic bacteria which may also be present (Ormerod and Friedmann, 1951; Rankin, 1953). Tissue invasion by this yeast and blood stream dissemination appear to be terminal events in most instances (Caplan, 1955; Mathias and Rees, 1956).

(2) *Actinomycosis*

Actinomyces israeli, included by custom among the pathogenic fungi, is, in fact, a filamentous micro-aerophilic bacterium. Under certain conditions of tissue damage or lung infection it produces one of the numerous manifestations of pulmonary actinomycosis which have been restudied by Bates and Cruickshank (1957). They proposed a new classification:

I. *Primary actinomycosis*

(*a*) *Pleuropulmonary* infection is the most common form of pulmonary actinomycosis. Where empyema alone presents, the prognosis is better than where lung also is involved.

(*b*) *Bronchopulmonary* infection is less common.

(*c*) *Mediastinal* disease may result from a lesion of the œsophageal mucosa. Infection may resolve, persist as a broncho-œsophageal fistula, or spread to the vertebral column or pericardium.

II. *Secondary actinomycosis*

(*a*) Extension from *abdominal* disease to one or other of the lower lobes of lung is the second most common cause of pulmonary actinomycosis.

(*b*) Extension from *cervico-facial* disease is more rare.

III. *Metastatic actinomycosis* of the chest wall or heart; *Pyæmia.*

IV. *Actinomycosis associated with pulmonary tuberculosis*

Actinomyces israeli and *Myco. tuberculosis* may occur together in empyemata.

Exogenously Acquired Infections

The fungi causing these diseases may be grouped under three headings:

(A) *Filamentous fungi* grow and may sporulate in the lung much as they do in nature or on nutrient media. They cause localised infections which only rarely disseminate (*e.g. Aspergillus fumigatus* (aspergillosis); *Rhizopus* sp. (mucormycosis)). *Nocardia asteroides* (nocardiosis) is strictly a filamentous bacterium and requires separate mention.

(B) *Yeasts* are unicellular fungi structurally suited to parasitism in tissues and to dissemination (*e.g. Cryptococcus neoformans* (cryptococcosis or torulosis)).

(C) *Dimorphic fungi.* These organisms, which are filamentous and sporing in nature, assume a yeast or other unicellular form in the tissues of hosts they infect. From the former sporing phase infection is readily

acquired, and by the latter tissue invasion is effected (*e.g. Histoplasma capsulatum* (histoplasmosis); *Coccidioides immitis* (coccidioidomycosis); *Blastomyces dermatititidis* (blastomycosis).

(A) *Infections due to Filamentous Fungi*

These organisms occur as contaminants and are not ordinarily pathogenic for man. Spores of harmless fungi are inhaled not infrequently in dust and may then produce fungus colonies in sputum cultures. They are particularly likely to be present in cultures of sputum from patients who have recently worked or resided in dusty spore-laden atmospheres. The repeated isolation of a fungus from sputa of a patient removed from his dusty environment may be indicative of fungal colonisation or invasion of bronchial or lung tissues. Table III records the filamentous fungi isolated at 37°C from sputa of the 1,060 patients referred to in Table I.

TABLE III

Filamentous fungus isolated	*No. of patients (1,060 examined)*	*% of patients*
ASPERGILLUS FUMIGATUS	55	4·7
Other fungi:	16	1·5
Aspergillus terreus	2	
Aspergillus niger	2	
Aspergillus flavus	1	
Aspergillus sp.	1	
Penicillium sp.	5	
Paecilomyces sp.	2	
Mucor sp.	1	
Unidentified	2	

From this group of patients, filamentous fungi were isolated with only about one-tenth of the frequency with which yeasts were grown. The prevalence of *A. fumigatus* in sputa is in sharp contrast to the frequency with which other fungi (*e.g. Alternaria, Penicillium* species) are present in the air. This difference in incidence cannot be explained entirely by the facility with which such fungi as *A. fumigatus* grow at 37°C. The respiratory tract appears, therefore, to be particularly suited to colonisation by certain fungi.

Bronchopulmonary Aspergillosis

This is caused almost invariably by *A. fumigatus*, though *A. niger* and certain other species of aspergilli have occasionally been implicated. Since *A. fumigatus* is a ubiquitous fungus associated particularly with decomposing vegetation (*e.g.* hay, straw and cereals), broncho-pulmonary aspergillosis tends to be most common amongst agricultural workers, gardeners and individuals feeding poultry and other birds. The ubiquity of this fungus makes for difficulty in assessing its significance when it is grown from sputum. In Table IV the

TABLE IV

Disease	*No. of patients with* A. fumigatus *in sputum* (1,060 *examined*)
Aspergillosis:	
Allergic type	7
Saprophytic type (mycetoma)	1
Bronchitis	12
Asthma	11
Pneumonia	7 (one patient with probable mycetoma)
Tuberculosis	2
Carcinoma	4 (one patient with confirmed mycetoma)
Lung abscess	2
Sarcoidosis	1
Cardiac disease	3
Other	5
Total patients with *A. fumigatus*	55 (4·7% of patients)

55 patients from whom *A. fumigatus* was isolated (Table III) are grouped according to the main disease for which they were receiving treatment.

This analysis deals with patients who showed *A. fumigatus* on one or more occasions in their sputum cultures, irrespective of whether the fungus was grown repeatedly from consecutive sputa, whether it grew profusely, or whether fungal filaments were seen by direct examination. Such additional observations are important, since the cultural isolation of *A. fumigatus* from a single sputum sample is usually without significance. On the other hand, where definite clinical evidence of aspergillosis exists, a single positive sputum culture of *A. fumigatus* provides useful contributory evidence as to ætiology. The incidence of *A. fumigatus* in sputa of patients in various disease groups is at present receiving study.

Whereas aspergillosis is a natural primary disease of birds simulating tuberculosis, it is doubtful whether infection is ever anything but secondary in man. There have been further British case reports since the comprehensive review of pulmonary aspergillosis by Hinson, Moon and Plummer was published in 1952. The disease takes one of three forms:

(*a*) *Saprophytic type.* Here *A. fumigatus* grows profusely in damaged bronchial or lung tissues and may be responsible for delayed healing and possibly toxæmia. The fungus may invade areas of unresolved pneumonia (Darke *et al.*, 1957), lung abscess (Hiddlestone *et al.*, 1951, Case 2; Stevenson and Reid, 1957), or asbestosis. Where cavitation is present, the fungus may produce sporing structures (Fig. 1). Zones of pulmonary infarction are very susceptible to aspergillus infection, as are lung or pleura damaged during surgery (Hiddlestone *et al.*, 1951, Case 1). Growth of *A. fumigatus* may also occur within ectatic bronchi (Hiddlestone *et al.*, 1951, Case 3), healing tuberculous cavities, and cavities associated with sarcoidosis or malignant disease; in such instances fungus growth is usually restricted to cavity lumena. A compact accumulation of fungus mycelium in these spaces gives rise to a so-called aspergillus "mycetoma" or "aspergilloma" having a characteristic

radiological appearance (Monod *et al.*, 1952; Bruce, 1957). Hæmoptysis is the important associated symptom. The ease with which the fungus may be grown from sputa of patients with mycetomata will depend on the freedom of communication between the fungus-containing cavity and the bronchial tree (Fig. 2). In the case illustrated by Fig. 3 several preoperative sputum cultures proved negative but cultures from the resected mycetoma (Fig. 4), though unusual, were all positive. Growth was atypical in being white and non-sporing (Fig. 5), though after prolonged culture scanty patches of greenish sporing areas typical of *A. fumigatus* developed. Similar observations were made on another mycetoma specimen recently examined.

(*b*) *Allergic type.* In this form of aspergillosis the fungus is present only scantily in affected bronchi, where it apparently excites the secretion of exudate temporarily obstructing the bronchial lumen. This exudate, which may be coughed up as " plugs " (Fig. 6), consists of mucus, fibrin, eosinophils. Curschmann's spirals, and Charcot-Leyden crystals; it can be shown to contain fragments of *Aspergillus* mycelium (Fig. 7). Episodes of collapse and consolidation of lung are sequelæ of the bronchial obstructions. Patients have a high blood eosinophilia and symptoms of asthma may be present. Citron (unpublished observation) has employed direct bronchial sensitivity tests for the investigation of these cases. This type of aspergillosis may be confused with pulmonary eosinophilia and with bronchiectasis complicated by pneumonia.

(*c*) *Septicæmic type.* Multiple abscesses or granulomata of the lungs develop in this rare form of infection.

Mucormycosis

Baker (1957) has drawn attention to a disease caused by another ubiquitous fungus, a *Rhizopus* species. Infection tends to complicate diabetes, leukæmia and debilitating diseases. Administration of corticosteroids and antibiotics may be other predisposing factors. Pulmonary mucormycosis, with or without hæmatogenous dissemination, is described.

Nocardiosis

Like actinomycosis, this is a bacterial infection and is caused by the partially acid-fast actinomycete, *Nocardia asteroides*. Nocardiosis differs from actinomycosis in being contracted by the inhalation of infected dust, though this does not appear to have occurred in Britain. In many respects the two diseases are similar, but in nocardiosis there is a greater tendency for dissemination.

(B) *Infections due to Yeasts*

Cryptococcus neoformans, an encapsulated yeast, is the only fungus in this group producing pulmonary disease. Not all strains of this organism are pathogenic and it is necessary to perform virulence tests on any strain isolated from sputum; this is, however, a very rare event.

Cryptococcosis (Torulosis)

There is no doubt that infection by *C. neoformans* can be acquired in Britain, presumably by inhalation of yeasts contained in dust. Saprophytic sources of the fungus have not been defined in this country, though *C. neoformans* has been isolated from milk (Carter and Young, 1950). Emmons (1951) in the United States has isolated the yeast from soil samples. *Cryptococcus neoformans* is an organism of low pathogenicity compared with such fungi as *Coccidioides* or *Histoplasma*; in contrast to what occurs with these latter fungi, laboratory infections due to *C. neoformans* are unknown. The occurrence of virulent *C. neoformans* in sputum is pathognomonic of disease; we know of only one possible exception in which neither bronchial nor pulmonary lesions were obvious. The incidence of subclinical infections is unknown, though there have been a number of unpublished reports of subpleural granulomata containing yeasts morphologically indistinguishable from *C. neoformans*. Unfortunately, skin tests and serological studies are of no help in diagnosis of cryptococcosis.

Intra-alveolar encapsulated yeasts may be demonstrated histologically in zones of pneumonitis caused by *C. neoformans*. Occasionally, the tissue response takes the form of localised granulomata, and cavitation may follow (Beck *et al.*, 1955, Case 2). Where unrestricted proliferation of yeasts occurs a tumour-like mass, or toruloma, results which may reach considerable size before signs or symptoms are produced (Cruickshank and Harrison, 1952). Encapsulated cryptococci were observed within caseous granulomata of the lung and suppurative lesions of spleen and liver in a patient described by Symmers (1953, Case 2). Rarely, disseminated lesions occur throughout the lungs as part of a blood-spread infection (Levene and Michaels, 1955). Dissemination of infection to meninges (Caldwell and Raphael, 1955; Kennedy, 1956), brain (Symmers, 1953, Case 1), skeletal system, and skin and lymph nodes (Symmers, 1953, Case 1; Misch, 1955) are well-recognised complications of this disease.

(C) *Infections due to Dimorphic Fungi*

These are acquired by the inhalation of spores in soil dust, at least in the case of histoplasmosis and coccidioidomycosis; blastomycosis has probably a similar ætiology. The diseases are benign in the great majority of instances and in many respects simulate tuberculosis both clinically and pathologically. They are virtually restricted to travellers from endemic areas, chiefly in the United States, and to laboratory workers handling cultures. Imported dusty materials should be considered a possible source of infection, particularly in a patient contracting one of these diseases who has not travelled outside Britain; in others endogenous reinfection may be important.

Histoplasmosis requires special mention in view of suggestions that infection may be acquired in Britain (Poles and Lavertine, 1954; Symmers, 1956). The population of this country has, however, a very low incidence of subjects giving a positive histoplasmin skin test so that this possibility would seem unlikely. It is made even less likely if Edwards (1957) is correct in her view

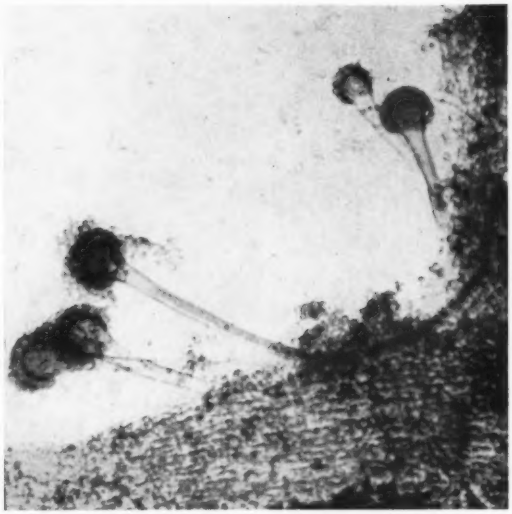

FIG. 1.—*Aspergillus fumigatus* invading cavitated area of unresolved pneumonia. Fungus filaments are seen lining the cavity and sporing structures are present within its lumen.

FIG. 2.—48-hour culture of sputum grown at 37°C. on Sabouraud's medium showing smoky-green colonies of *Aspergillus fumigatus* and also *Candida albicans* colonies.

To face p. 40

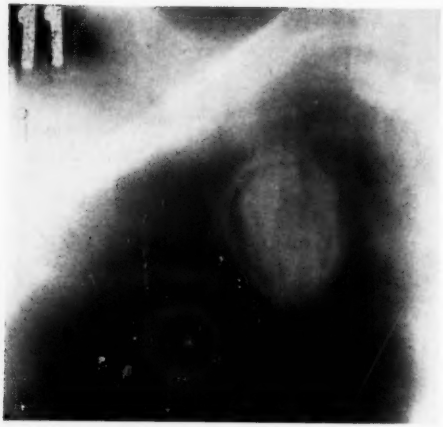

FIG. 3.—Aspergillosis of lung. A male, age 41, found to have a lung lesion by mass miniature radiography. History of pain in the chest and haemoptysis. Tomography of right upper zone shows rounded opacity with a thin crescent of air almost completely surrounding a central mass.

FIG. 4.—Resected specimen from patient referred to in Fig. 3 showing lobulated mycetoma in cavity with smooth lining.

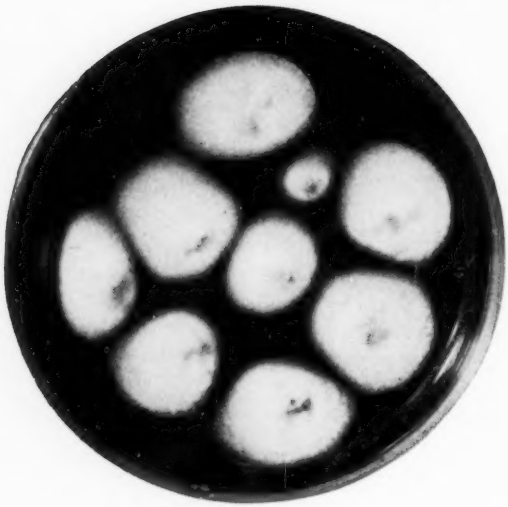

FIG. 5.—5-day culture of poorly sporing variant of *Aspergillus fumigatus* grown from a mycetoma (Fig. 4).

FIG. 6.—"Plugs" and casts in sputum from a patient suffering from allergic type of bronchopulmonary aspergillosis.

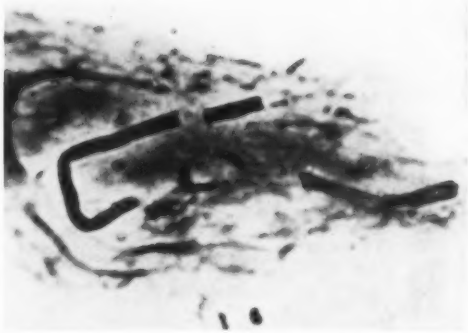

FIG. 7.—Fragmented filaments of *Aspergillus fumigatus* present in sputum plugs seen in Fig. 6. (Stained by silver impregnation.)

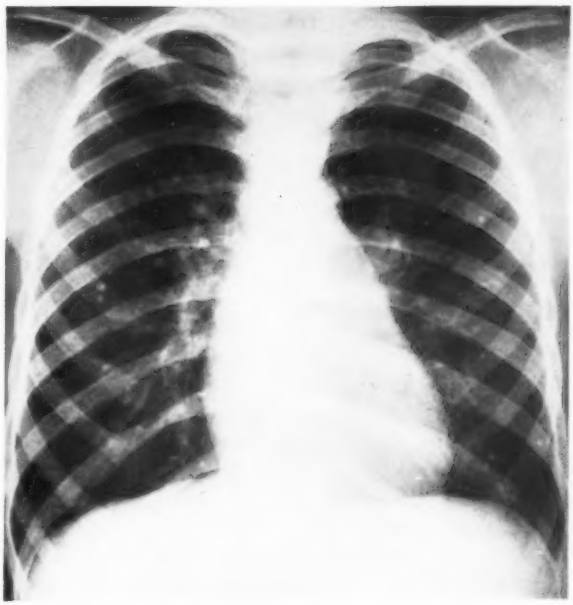

FIG. 8.—Healed asymptomatic histoplasmosis. A female child, age 6, without abnormal signs or symptoms apart from recurrent cough. Histoplasmin skin test positive and Mantoux negative. History of 2 years residence in Toronto with mother who is also histoplasmin positive; a sister who has never been away from Britain is insensitive to histoplasmin. Radiograph shows 2-3 mm. well-defined circular shadows of high density.

that the usually adopted 5 mm. criterion for a positive histoplasmin skin test will tend to overestimate the percentage of infected persons in zones of low endemicity. The existence in Britain of localised areas of soil contamination by *Histoplasma* must, however, be considered a remote possibility. It is of interest that within certain areas of the United States having low incidence of histoplasmin sensitivity small pockets of high incidence have been described and *H. capsulatum* isolations from soil connected with them.

Skin tests similar to the Mantoux test will detect past or present infections by dimorphic fungi. Serology may be used to discover early infections and to assess activity of disease. An anamnestic response following pneumonia was recorded by Leigh and Thomas (1955).

Histoplasmosis

This is caused by *Histoplasma capsulatum*. The fungus grows in nature, and in culture at room temperature, as filaments producing tuberculate spores, but when it becomes parasitic in tissues or is grown on enriched medium at 37°C. it changes to minute yeasts. In tissues these are essentially intracellular parasites. *Histoplasma capsulatum* has not been found in nature in Europe, though in the United States it has been isolated from the soil (Grayston and Furcolow, 1953) and from the air (Ibach *et al.*, 1954). In Britain, approximately 12 cases of histoplasmosis have been recorded during the last ten years; several other probable examples of healed disease have been seen but not reported. All except the patient described by Symmers, 1956, had travelled abroad at some time prior to onset disease, either to a known endemic area of North America or to the Middle or Far East. In three instances (Hutchinson, 1952; Lockett *et al.*, 1953; Poles and Lavertine, 1954) patients had been continually resident in Britain for several years before histoplasmosis became manifest. These British reports will be referred to under the types of disease described by Furcolow (1956).

1. *Asymptomatic infections.* Infection may occur at any age and even brief residence in an endemic area is important in case histories. It is estimated that pulmonary lesions demonstrable radiologically are present in at least one-third of cases. These often calcify slowly (Fig. 8) and are then usually indistinguishable from healed miliary tubercles. A preponderance of discrete and perfectly spherical lesions should, however, suggest histoplasmosis. Possible examples of healed asymptomatic histoplasmosis have been reported (Crofton, 1954; Leigh and Thomas, 1954), but these may originally have been cases of acute epidemic disease.

2. *Mild or moderately severe histoplasmosis.* Mild infections causing influenza-like symptoms last from one to four days; signs and symptoms of pulmonary involvement are usually absent. There are radiological changes of nodular type in about two-thirds of cases and healing lesions often calcify; the patient described by Arblaster (1950) was presumed to be in this category. About one-third of cases show diffuse pulmonary infiltration; less commonly lymph nodes only are involved.

Moderately severe infections may be confused with atypical pneumonia.

In these cases, illness lasts from five to fifteen days, is of sudden onset with malaise, lassitude, cough, chest pain and fever rising to 104°C., and relapses not infrequently occur. *Histoplasma capsulatum* may be cultured from the sputum, and in most cases both the histoplasmin skin test and serological studies give positive results by the third or fourth week of disease. Serum titres then decrease but may still be significantly raised after one year. Exposure to garden or farm soil contaminated by chicken excreta two weeks prior to illness has been a feature of some of these infections (Kier *et al.*, 1954).

3. *Severe histoplasmosis.*

(*a*) *Acute epidemic disease.* This type affects families or groups of people having a common exposure to a source of infected dust (Furcolow and Grayston, 1953). Fever and prostration occur often without symptoms referable to lungs; radiological evidence of diffuse pneumonitis is usually present by the third week. Histoplasmin skin tests and serology are positive. Recovery is the rule weeks or months after onset of disease. The final calcified phase similar to that reported by Crofton (1950) and Leigh and Thomas (1954) is usually an unexpected radiological discovery some years later.

(*b*) *Acute progressive disease* lasts a few weeks only and terminates fatally with blood-spread to most organs. It tends to occur at extremes of age and in patients debilitated by carcinoma, leukæmia, or tuberculosis. High fever, hepatomegaly and splenomegaly develop but there is little radiological change in chest X-rays; blood and marrow cultures are usually positive for *H. capsulatum.* Histoplasmin skin tests may be negative in very ill patients but serological tests are usually positive. Disease sometimes presents as a mucosal lesion of the mouth, throat or larynx as in the case described by Lockett *et al.* (1953); this patient had visited Egypt, India and South Africa, but had lived in Britain continuously for seven years prior to diagnosis. The patient described by Poles and Lavertine (1954) had visited France, Nigeria and Burma, but had resided in Britain during the six years prior to onset of laryngeal disease thought at first to be tuberculous in nature. Laryngeal histoplasmosis may also mimic carcinoma as in Hutchinson's case (1952); in this instance residence in Britain had been continuous for fourteen years prior to onset of symptoms, though there was a history of extensive travel in the tropics.

(*c*) *Chronic progressive disease* simulates chronic fibro-cavitary tuberculosis and tends to occur amongst older persons. It has been diagnosed not infrequently amongst patients in tuberculosis sanatoria in the United States. *Histoplasma capsulatum* can usually be cultured from the sputum; skin and serological tests are positive. Edge (1958) has reported a possible example of this type of disease in Britain.

(*d*) *Reinfection histoplasmosis.* There is increasing evidence of the occurrence of endogenous and exogenous reinfection.

(*e*) *Histoplasmosis complicating other diseases.* Symmers (1956) has reported histoplasmosis of supraclavicular lymph nodes in a patient suffering from sarcoidosis; the patient was symptomless sixteen months after mycotic lymphadenitis was diagnosed. This is believed to be the first example of mycologically proven histoplasmosis in a person who had never travelled outside Britain.

Coccidioidomycosis

Coccidioidomycosis caused by *Coccidioides immitis* very closely mimics tuberculosis. The only published British report is that by Nabarro (1948), a case of severe though benign primary pneumonitis in a laboratory worker. Our own experience in Britain is limited to studies of the fungus isolated from the sputum of an American serviceman found by routine radiography to have a thin-walled pulmonary cavity, a well-recognised sequela of primary disease.

Blastomycosis

Dowling and Elworthy (1925) described a patient with dermal lesions caused by *Blastomyces dermatitidis;* no physical signs of pulmonary disease were found. It was noteworthy that this man had been handling packing cases from the United States. Symmers (1956) quotes a case of pulmonary blastomycosis seen in Britain.

Summary

Fungous diseases of the lung occurring in Britain are reviewed. The incidence and significance of *C. albicans* in sputum is considered. Bronchopulmonary aspergillosis, cryptococcosis (torulosis) and histoplasmosis are discussed as being mycotic diseases of interest in Britain.

Case material of Figs. 3 and 4 are shown by courtesy of Dr. F. H. Young and Mr. Norman Barrett, and Fig. 10 by courtesy of Dr. C. P. Pinckney.

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PULMONARY HISTOPLASMOSIS

By J. R. Edge

From the North Lonsdale Hospital, Barrow-in-Furness*

Histoplasmosis is an acute, subacute or chronic infection caused by the fungus *Histoplasma capsulatum* which exists in two forms, the mould-like (saprophytic) phase growing at 22° C., and the yeast-like (parasitic) phase growing on enriched media at 37° C. (Riddell, 1951). The saprophytic form is found mainly in soil and animal excrement, while the parasitic form is seen typically in the tissues of infected humans or other animals. One fungal form is transformed into the other by a change in environment, and it follows that histoplasmosis frequently occurs in those in contact with infected soil or excreta. Infection is believed to occur both by inhalation and ingestion, but man to man infection has not been demonstrated.

From the considerable recent literature concerning histoplasmosis, mainly from the United States, it appears that the disease may present in a variety of ways, ranging from sub-clinical cases, which are the commonest (Palmer, 1945), through more or less benign acute or chronic pulmonary forms, to the acute generalised and progressive systemic disease (Furcolow and others, 1947; Bunnell and Furcolow, 1948; Christie, 1951). The relative incidence of the generalised and pulmonary types is unknown, but in the United States at least the disseminated form appears to be rare, whilst the pulmonary variety is relatively common. In all these phases the differential diagnosis from tuberculosis may be difficult.

Fourteen patients have been previously diagnosed in Britain. Five, all of whom had visited North America, had calcified pulmonary lesions only (Crofton, 1950; Arblaster, 1950; Sakula, 1953; Lee and Thomas, 1955). Seven had all previously lived in Africa or the East; of these, three had the generalised progressive disease (Derry and others, 1942; Locket and others, 1953; Poles and Lavertine, 1954); three had cutaneous (Duncan, 1947; Symmers, 1956) and one laryngeal (Hutchison, 1952) lesions. Only two patients had never left Britain; in one the fungus was isolated in culture from an enlarged cervical lymph node (Symmers, 1956 (1)); the other presented as an abscess in the right iliac fossa six weeks after appendicectomy, and must be regarded as unproven (Limerick, 1951).

In the present paper a further two examples of possible pulmonary histoplasmosis are described, occurring in a married couple who had lived

* From a paper read before the Thoracic Society, London, on March 2, 1955.

(*Received for publication November 11th*, 1957.)

in Ohio from 1926 to 1934 and then returned to live in North Lancashire. There is no history of any illness of note during their stay in the United States.

Case Reports

CASE 1. Mrs. A., a housewife, born in 1902, was first seen in 1951. For about twenty years she had had recurrent cough, and wheeziness in damp weather, and exertional dyspnœa had been progressive; for the last three years she had been virtually crippled by dyspnœa, being able to walk only very slowly on the level. She denied having any febrile chest illness, nor had she ever had to retire to bed because of her chest. There was no history of any other illness of note.

The chest was first X-rayed in 1951 after a small hæmoptysis, when the film showed scattered linear, nodular and coalescing shadows in all zones of both lungs (Fig. 1). A right lateral picture showed bullous emphysema in the right upper and middle lobes. Further X-rays until her death in November 1956 showed no substantial change. On tomography no definite enlargement of the hilar glands was seen; the bones of the hands and feet were radiologically normal.

She was admitted to hospital in May 1954 for investigation.

ON EXAMINATION. The facies was plethoric, with central cyanosis more marked in the presence of bronchospasm. Movement of the chest was limited, and the breath sounds were reduced. Finger clubbing was absent and the larynx was normal. The liver and spleen were not palpable, nor were there any significantly enlarged lymph nodes. There was no evidence of heart failure.

SKIN TESTS. The Mantoux test was positive ($\frac{1}{1000}$ O.T.), and intradermal injection of $\frac{1}{10}$ c.c. of $\frac{1}{100}$ histoplasmin was followed by redness and induration, reaching a maximum diameter of 22 mm. on the third day. A coccidiodin test produced only a transient flare, without induration. The histoplasmin test was repeated four months later and on this occasion the reaction was more strongly positive, with induration 35 mm. in diameter.

BACTERIOLOGY. Many specimens of sputum and gastric washings were negative for tubercle bacilli, both on direct examination and culture, and a further fifteen specimens of sputum and three of gastric washings were also negative for *Histoplasma capsulatum* by culture on Sabouraud's medium.

SEROLOGY. The collodion agglutination test for histoplasmosis was negative, and the histoplasma complement fixation test was positive to a titre of only 1 : 80, considered to be insignificant. The blood Wassermann reaction was negative.

OTHER INVESTIGATIONS. Examination of the blood showed a moderate polycythæmia (hæmoglobin 110 per cent.; red cell count 6,000,000 per cubic mm.); on one occasion only there was significant eosiniphilia (520 per cu. mm.). The serum proteins were normal, and sternal marrow and liver biopsies were within normal limits, there being no evidence of histoplasmosis. An electrocardiogram showed marked right ventricular preponderance.

While the positive skin tests in this patient indicated that histoplasma infection had occurred, the interpretation of the radiographs is debatable. Such extensive changes may result from chronic bronchitis, but were this the cause one would expect a history of many febrile illnesses associated with recurrent

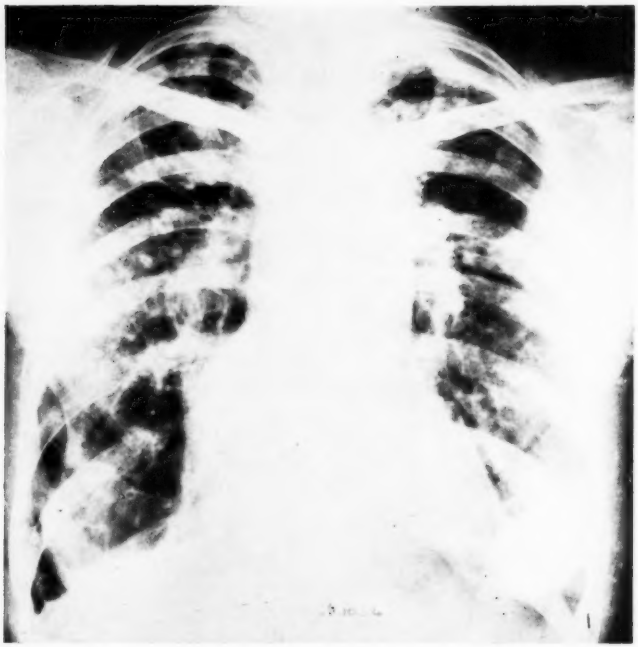

FIG. 1.—Case 1. Postero-anterior chest radiograph.

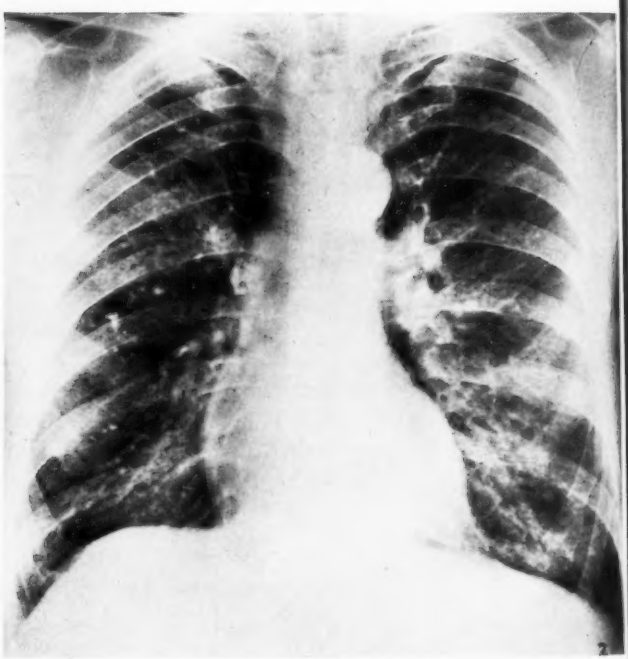

FIG. 2.—Case 2. Postero-anterior chest radiograph.

To face p. 47

pulmonary infection; there was no such history in this case. Although she suffered from spasmodic asthma in childhood, it seems improbable that this alone would have caused these changes. There was no evidence to support a diagnosis of healed sarcoid lesions.

She was readmitted to hospital on 28.9.56 with right-sided heart failure from which she died on 13.11.56.

Pathology

The heart, lungs, parts of liver, spleen and kidney were examined by Dr. Lynne Reid, who reported as follows:

" *Macroscopic Appearances*

Lungs. There was no evidence of disease in the hilar lymph nodes.

Large bullæ were present at the base of the left lower lobe and along the anterior edge of the right middle lobe, while smaller bullæ were found irregularly scattered through other parts of the lung. Over each lobe between one and three plaque-like areas of pleural thickening, varying in size from 5 cm. to 10 cm. in diameter, were present. Nodular lesions deep in the lung were identified by palpation and excised in order to obtain material for culture, both for *Myc. tuberculosis* and for *Histoplasma capsulatum*, after which both lungs were sliced. It was then seen that throughout the lower lobes and the inferior part of the upper lobes there were scattered areas of emphysema with bullæ, and many scars both in the subpleural and deeper regions, although there were also large areas which macroscopically appeared normal. There was no evidence of necrosis, caseous or otherwise, nor of cavitation.

Histology. The *spleen* and *kidneys* showed no abnormality.

The *liver* showed loss of lobular arrangement and a well-developed fine cirrhosis.

Lungs. Sections of all lobes were examined and showed extensive dense scarring, frequently subpleural, some scars, judging by the size of the supplying bronchus, representing a considerable volume of normal lung. Some scars were associated with gross emphysema, while adjacent to others the lung was normal. There was considerable endarteritis of some branches of the pulmonary artery supplying the scarred parts of the lung.

Nine separate specimens were examined by smear and culture for tubercle bacilli and *Histoplasma capsulatum*, with negative result.

Sections from each block were stained by hæmatoxylin-eosin, periodic acid Schiff and Verhoeff van Gieson methods. There was no evidence of any specific disease; no fungi, bacteria, nor any significant number of eosinophils being seen in the sections. In the areas of fibrosis elastic stains showed that sometimes there was collapse and sometimes organisation of intra-alveolar exudate.

The damage to the lungs was more marked at the bases than at the apices and the absence of caseation or specific granulation tissue made sarcoid and, even more, tuberculosis unlikely diagnoses. The absence of infolding of the pleura at the areas of scarring and of the typical tangle of elastic fibres in the histological sections precludes multiple infarction as a cause of damage.

Since little is known of the pathological changes seen in the later stages of this disease, nor of the possibility of complete healing, histoplasmosis cannot

be excluded, although, in the absence of necrosis or fungi, the picture is entirely non-specific. The pneumonic condition of the lungs sometimes seen in patients with asthma with or without eosinophilia in the blood is another possible cause of this pulmonary damage."

CASE 2. Mr. A., born in 1898, had always enjoyed good health; he was first X-rayed in 1954 in the course of investigating his wife's illness. The film shows numerous small round calcified opacities in the right mid and lower zones, with a large calcified hilar lymph node (Fig. 2). His histoplasmin test was violently positive, with very striking œdema and redness of the whole forearm; there was a plaque of induration 34 mm. in diameter after forty-eight hours, with a central vesicle 3 mm. across. The test was repeated four months later and was followed by an even more violent local reaction, the blister this time measuring 20 mm. in diameter. The tuberculin test was positive and the coccidiodin test negative; the collodion agglutination test for histoplasmosis was negative.

Whilst the X-ray appearances would be in keeping with a diagnosis of healed primary tuberculosis, the multiple pulmonary lesions and the irregular appearance of the hilar gland are well known to occur in healed pulmonary histoplasmosis. He was a keen and active gardener throughout his stay in America, and could conceivably have inhaled infected dust in his garden.

The patient's daughter was born in Youngstown in 1931, and left at the age of $2\frac{1}{2}$ years. Her chest X-ray is normal and the histoplasmin skin test negative.

THE DISTRIBUTION OF HISTOPLASMIN SENSITIVITY

Attention was first drawn to the frequent occurrence of pulmonary histoplasmosis in certain parts of the United States by Palmer, and Christie and Peterson, in 1945; these authors investigated a large number of persons discovered during mass X-ray surveys to have pulmonary infiltrates, or calcified

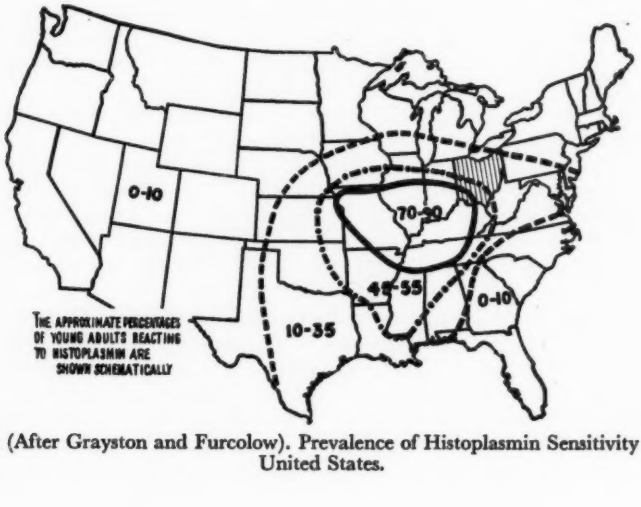

Fig. 3. (After Grayston and Furcolow). Prevalence of Histoplasmin Sensitivity in the United States.

shadows, indistinguishable from tuberculosis. Many of them had negative tuberculin tests but were found to react to intradermal histoplasmin, and from a small proportion of these the fungus was isolated by culture of sputum or gastric washings; the very large majority were symptom free. Since then the prevalence of histoplasmin skin sensitivity has been widely investigated in the United States (Grayston and Furcolow, 1953) and on a smaller scale elsewhere (Mochi and Edwards, 1952; Stott, 1954).

The incidence is highest in the East Central part of the United States, where between 70 and 90 per cent. are reactors (Fig. 3, after Grayston and Furcolow, 1953). Ohio is seen to lie at the north-east tip of this area of maximum prevalence. The writer is indebted to Dr. Carrol Palmer for further information regarding the distribution of histoplasmin sensitivity in Ohio (Fig. 4); there is a prevalence of reactors of up to 90 per cent. in the south-

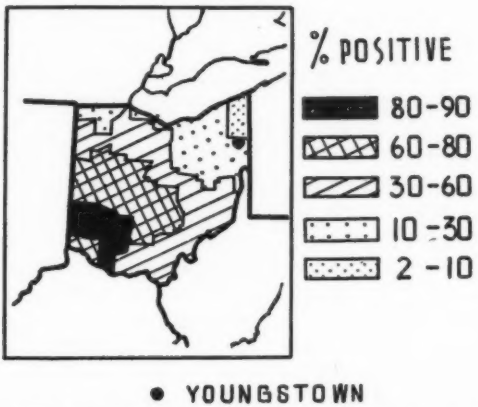

Fig. 4. (By courtesy of Dr. Carrol Palmer). Distribution of Histoplasmin Sensitivity in Ohio.

west of the State, which tails off to under 10 per cent. in the north-east; Youngstown, where both patients lived for nine years, lies in the area with a prevalence of between 10 and 30 per cent. These figures were obtained by skin testing sample populations of lifetime residents; of 1,211 persons resident within 50 miles of Youngstown who were tested, 160 (13 per cent.) were positive reactors (Palmer, 1954).

No positive histoplasmin reactors have been discovered amongst some 4,000 permanent residents in Britain who have been tested (McCracken, 1948; *Lancet*, 1949; Riddell, 1955), excepting only the patient described by Symmers (1956 (1)).

Diagnosis

Isolation of the organism during life in pulmonary histoplasmosis is evidently difficult, as in Furcolow's (1947) series, in spite of intensive efforts, a positive culture was recovered in only one of the seventy-nine subjects investigated. Bunnell and Furcolow (1948) report on ten proven cases of

histoplasmosis, selected from a "large group" of persons studied over a period of two-and-a-half years, and in only three of these patients was the disease apparently limited to the lungs; the organism was cultured from the sputum in one and from gastric washings in two. In contrast, isolation of the fungus from the soil or animal excreta appears to present less difficulty. Thus Grayston and Furcolow (1953) describe thirteen outbreaks of acute respiratory illness in men working amongst soil, or animal excreta, and in eleven of these *Histoplasma capsulatum* was isolated from material taken from the place of work. The attack rate among these workmen was high (about 90 per cent.); the histoplasmin test was positive in all patients on whom it was used; and the chest radiographs showed mainly scattered broncho-pneumonic types of lesion. A further case of acute bronchopneumonic histoplasmosis, with complete recovery, is described in detail by Kier and others (1954); this patient became ill shortly after sifting a load of soil delivered to his garden, from which the fungus was later isolated.

More often the diagnosis must depend on the histoplasmin skin test, particularly where the tuberculin test is negative (Palmer, 1945; Furcolow and others, 1947; Christie, 1951); and on serological tests (Furcolow and others, 1948; Campbell, 1955). Both are regarded as highly specific; although in the case of the skin tests cross-reactions with coccidiodin (Mochie and Edwards, 1952) and blastomycin (Christie, 1951) may sometimes occur, these are probably not of great practical significance; and cross-reactions with tuberculin are thought to be extremely rare (Palmer and Strange Petersen, 1950). The serological tests—*i.e.*, collodion agglutination and histoplasma complement fixation tests—are of most value during the first months after infection, as later the antibodies tend to disappear (Campbell, 1955).

As the incidence of tuberculin sensitivity in Lancashire is very much greater than in those parts of the United States where the problem of histoplasmosis has been most widely investigated, it is felt that the positive tuberculin tests in the present patients have no bearing on the diagnosis. The serological tests would be expected to be negative at so long an interval after infection had taken place.

The Natural History of Pulmonary Histoplasmosis

Although acute chest symptoms are not unusual during the first weeks after infection, prolonged ill-health due to pulmonary histoplasmosis is uncommon; and in the majority of cases the disease runs an entirely benign course. Thus Furcolow and others (1947) described a series of seventy-nine children aged 4 to 18 years, investigated in Kansas City, who had abnormal X-ray shadows associated with negative tuberculin and positive histoplasmin tests; seventy-two of the children were free of symptoms. Several of these patients had patchy diffuse lesions scattered through both lungs, and the authors remark that this type of disease is exceedingly chronic, though they are unable to say how long it might continue without calcification; in a four-year follow up of a similar group of children Furcolow (1949) found

that calcification had occurred in the majority, the remainder having either cleared completely or proceeded to fibrosis; in none of these children had the lesions progressed. The finding of a positive skin test with calcified lesions is, in the view of these authors, characteristic, and they believe that skin sensitivity is frequently permanent.

The findings in the present subjects, who appear to provide an unusual opportunity for the study of this disease twenty years after removal from the source of infection, are in keeping with this experience. In the one case, there were very chronic lesions scattered throughout both lungs leading to fibrosis and emphysema, and in the other completely calcified lesions; both patients showed a strongly positive skin test to histoplasmin.

Summary

A woman of 55, who lived in Ohio from 1926 to 1934, and has since lived in Lancashire, was found to have scattered infiltrates and fibrotic changes throughout both lungs, associated with a strongly positive histoplasmin test. She died of cor pulmonale after many years of respiratory crippling: pathological examination of the lungs showed gross fibrosis with emphysema.

Her husband, who lived in Ohio for a similar period, has scattered calcified opacities in the right lung, with a calcified hilar gland, and a violently positive histoplasmin test. He is entirely free of symptoms.

The possibility is presented that these radiological changes are consequent upon infection with *Histoplasma capsulatum* acquired during the patients' residence in the United States. The extensive studies of this disease in the United States during the last ten years, arising from the importance there of pulmonary histoplasmosis in the differential diagnosis of tuberculosis, are briefly reviewed.

It is a pleasure to acknowledge by indebtedness to Dr. Carroll Palmer for Map 2 (Fig. 4) and for kindly providing me with information regarding the prevalence of Histoplasmin sensitivity in Ohio; to Dr. J. E. Horrocks for his help in investigating these patients; to Dr. R. W. Riddell for his great interest and encouragement; to Dr. Lynne Reid for the pathological report; and to Mr. D. Kemp, Photographic Department, Institute of Diseases of the Chest, for the photographs.

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TENSION CYSTS OF THE LUNG IN INFANCY AND CHILDHOOD

By R. H. R. Belsey

From the Department of Thoracic Surgery, Frenchay Hospital, Bristol

The term "tension cysts" should embrace all cystic conditions of the lung in which the contents are contained under a positive pressure sufficient to result in compression or collapse of surrounding lung tissue, and displacement of the mediastinum. It is upon the presence of these secondary changes that the clinical diagnosis is based. Seldom is it safe or practical to measure directly the intra-cavitary pressure.

The contents may be air or fluid. Air can only be trapped in a cyst as a result of the existence of a "ball valve" obstruction in the bronchus or bronchioles communicating with the cyst. Air enters the cyst during inspiration only to be trapped as the bronchus becomes completely occluded during the normal physiological contraction occurring during expiration. The absorption of air from the cyst and its replenishment during forced inspiration is probably occurring continuously. The actual pathology and site of the obstruction is difficult to determine even by serial section of excised lobes.

Minimal changes in local pathology can completely change the situation. If the obstruction becomes complete the cyst will empty owing to absorption of the contained air. If the expiratory obstruction disappears the tension will collapse and the intra-cavitary pressure will become the same as that in the surrounding lung tissue.

The direct measurement of intra-cavitary pressure by inserting a needle into the cavity can only be performed with safety in the presence of an obliterated pleura and the clinical determination of pleural adhesions is difficult or impossible. If the cyst is needled across a free pleura a tension pneumothorax may rapidly supervene and embarrass the child still further. The measurement of intra-cavitary pressure calls for an isometric technique, as the escape of even a minimal quantity of air into the manometer or measuring apparatus will invalidate the results.

Fluid-containing cysts can result only from the existence of secreting cells in the cyst lining or as the result of infection in the absence of any open communication with the bronchial tree. However, it is the air-containing cysts that present the greater interest in view of the diagnostic problems involved, the dramatic complications, and the urgency of surgical treatment in most cases.

Included in the term tension cysts will be other tension phenomena, such as obstructive emphysema from various causes, which have similar effects on

(*Received for publication July* 26, 1957.)

surrounding intra-thoracic structures by virtue of their action as expanding space-occupying lesions, which can only be differentiated with great clinical difficulty from true cystic conditions, and often call for the same treatment.

The danger to the patient stems from the fact that in a relatively closed space such as the thoracic cage the expansion of one segment or lobe of lung tissue can only occur at the expense of adjacent segments and other structures such as the large venous channels and atria, with pressure collapse, diminished ventilation and cardio-vascular embarrassment. Moreover, the accumulation of a positive pressure within a lobe may occur with great rapidity and a correspondingly dramatic interference with the cardio-pulmonary function. Finally, the evidence of the cases reported herewith points to the irreversible nature of the pressure build-up in the majority of cases, and a fatal termination unless the tension can be promptly released or the ballooned segment excised.

Theoretically, at the end of full inspiration any positive pressure gradient between the cyst contents and the surrounding lung tissue should disappear, and the mediastinum should return to the midline. In fact this does not occur and it might appear difficult to attribute the phenomena solely to the trapping of inspired air. When the cyst has acquired such a size and tension that surrounding segments become atelectatic, the fall in intrathoracic pressure during inspiration will deflect an increasing proportion of the inspired air into the cyst owing to the loss of elasticity of the adjacent atelectatic segments and the relatively enormous resistance to re-expansion offered by the surface tension of the opposed alveolar walls. The factors limiting the ultimate expansion of the cyst may not become operative before a fatal stage of cardio-pulmonary embarrassment has been reached.

Any cystic condition of the lung that has acquired a communication with the bronchial tree may at any time develop a positive pressure when the size of the communication is such that intermittent opening and closure occurs during the normal respiratory cycle.

Diagnosis of the tension phenomenon is based on the shift of the mediastinum away from the lesion, occasional bulging of the chest wall, hyper-resonance and the absence of air entry. The differentiation of the various types of tension cyst may be suggested by X-ray changes, but the difficulties are notorious and much will depend upon the perfection of the radiological technique. The differential diagnosis lies mainly between contra-lateral atelectasis with gross compensatory emphysema, spontaneous tension pneumothorax, obstructive emphysema and congenital diaphragmatic herniæ. The rapid deterioration of the infant may preclude any intensive investigation such as a barium meal to eliminate a diaphragmatic hernia, and the diagnosis must usually be based on the history, the physical signs such as the presence or absence of bowel sounds, and the interpretation of radiological appearances. The radiological differentiation between obstructive emphysema and a tension pneumothorax, or between a loculated tension cyst and a congenital diaphragmatic hernia, may elude even the most experienced radiologist.

Diagnostic tapping of the chest affords little or no useful information and may be dangerous, by adding a pneumothorax to an already desperately

embarrassed child if the tension cyst is punctured by the needle across a free pleural space.

The diagnosis may only be completed at the time of an exploratory thoracotomy. In the newborn infant neither time nor the patient's condition will permit bronchoscopy, and the information obtained by this examination rarely influences the surgical programme. In the older child, however, bronchoscopy is essential to exclude a foreign body causing obstructive emphysema of a lobe or lung before other causes of the tension phenomenon are sought.

Treatment can rarely be directed at the ball valve mechanism responsible for the tension phenomenon, owing to its inaccessibility. In the majority of cases the only logical treatment available is excision of the obstructed segment of lung tissue. This may have to be performed as an acute emergency and the decision to perform a thoracotomy must not be delayed till the infant is moribund. Anæsthesia presents a formidable problem owing to the grossly diminished pulmonary ventilation and the difficulty of inflating the collapsed contra-lateral lung. Once the chest has been opened the obstructed segment may be delivered through the wound, or a solitary cyst incised with dramatic relief, and the anæsthetist's problems are then largely overcome.

Infants and children tolerate a thoracotomy very well. The excision of the obstructed or cystic segment or lobe is rarely difficult technically, except in those cases where there has existed previous inflammation. Convalescence following resection should be rapid and smooth. Open drainage plays little or no part in the management of tension cysts, as complete healing is unlikely to occur and the build-up of positive pressure may recur as soon as drainage is discontinued. On the other hand, some form of temporary drainage, by a two-stage method in the presence of a free pleura, may tide the child over and assist the anæsthetist when a thoracotomy is performed.

Classification

The causes of tension phenomena can be classified as follows:

(i) Developmental cysts.
(ii) Infective cysts.
(iii) Obstructive emphysema due to:

- (*a*) Atresia of a bronchus.
- (*b*) Atresia of the bronchioles.
- (*c*) Inflammatory stricture of a bronchus.
- (*d*) Foreign body.
- (*e*) Bronchial tumours—very rare in childhood.

Developmental Lung Cysts

The embryology of these cysts is imperfectly understood and no useful purpose can be served by reviewing the various theories concerning their evolution. The cysts may be solitary, multilocular or multiple. The multiple

cysts may be confined to one lobe or may be diffusely scattered throughout both lungs. They are rare, and seldom complicated by tension phenomena, but the author has seen one child of two years with a bilateral pneumothorax complicating diffuse cystic disease of both lungs, possibly due to spontaneous rupture of cysts that had acquired a positive pressure. It is usually the solitary or multilocular cyst that presents the tension phenomenon. The cyst is lined by typical ciliated columnar bronchial epithelium. Other cases have been seen in which the cyst is lined by a simple flattened epithelium of indeterminate nature and there is some doubt as to whether these should be classified along with the former group, although in every other respect they are similar.

If tension is going to occur in the developmental cyst it usually does so within the first week or two of life. The infant appears normal at birth but within a few days develops dyspnœa and cyanosis, and its general condition rapidly deteriorates. Physical examination reveals bulging of the chest wall on the affected side and a gross shift of the mediastinum towards the opposite side. Air entry is poor over the whole chest. The absence of bowel sounds does not exclude a diaphragmatic hernia. Only perfect radiological technique and the enlightened interpretation of films of varying intensity will differentiate between a tension cyst, obstructive lobar emphysema and a tension pneumothorax. It is highly dangerous to needle the chest unless the clinician can be reasonably certain a pneumothorax is present. The decision regarding treatment is a matter of extreme urgency owing to the imminent suffocation of the child. In the author's experience the tension phenomenon is an irreversible process and spontaneous relief is very unlikely to occur. An immediate thoracotomy should be performed, the diagnosis confirmed, and the ballooned lobe, or lung, excised.

A tension cyst may occur in association with sequestration of a lobe. Technical difficulties may arise during excision, due to the abnormal systemic arterial supply from the thoracic or abdominal aorta to the sequestrated lobe.

Case 1. P.J. Male, aged 11 days. Well for first seven days. Sudden attack of cyanosis and dyspnœa on ninth day of life. X-ray (Fig. 1, Plate V) revealed tension cyst in left chest. Barium meal showed no evidence of diaphragmatic hernia. A needle had been inserted into the chest at another hospital and a positive pressure of 10 cm. of water recorded. The infant's condition improved temporarily after the withdrawal of 150 c.c. of air, but soon relapsed. The cyanosis was not relieved by administration of oxygen.

17.5.50. Left thoracotomy and total left pneumonectomy performed on day of admission. A large multilocular tension cyst occupied the left lower lobe; the upper lobe appeared mal-developed, and could not be inflated. Uneventful convalescence.

Pathologist reported: "Trabeculated cyst lined with cubical and low columnar ciliated epithelium; smaller cysts present in surrounding lung tissue."

Case 2. P.B. Male, aged 3 months. Normal birth. Began to cough at age of three weeks; cough had persisted. X-ray (Fig. 2, Plate V) suggested congenital right-sided diaphragmatic hernia. Barium meal revealed no hernia.

PLATE V

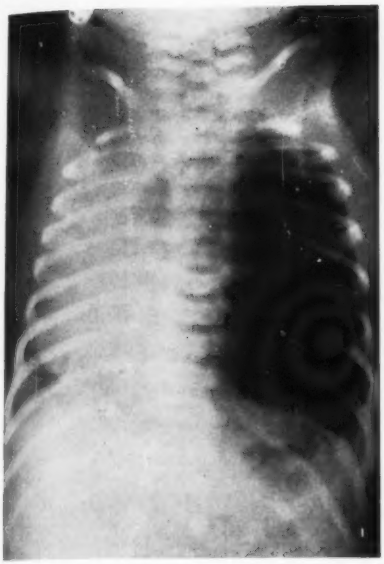

FIG. 1.—Case 1. Tension developmental cyst of left lower lobe, causing gross mediastinal shift and collapse of the right upper lobe.

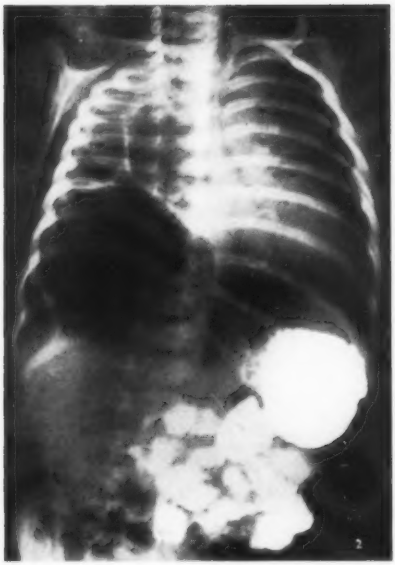

FIG. 2.—Case 2. Tension cyst of right lower lobe; heart displaced to the left. Diaphragmatic hernia excluded by barium meal and follow-through.

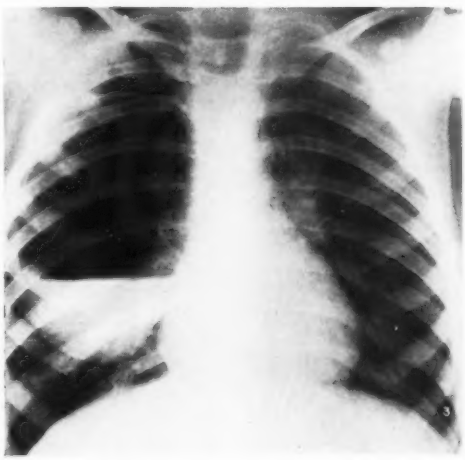

FIG. 3.—Case 3. Developmental cyst of right upper lobe. No evidence of any positive pressure phenomenon at present time.

To face p. 56

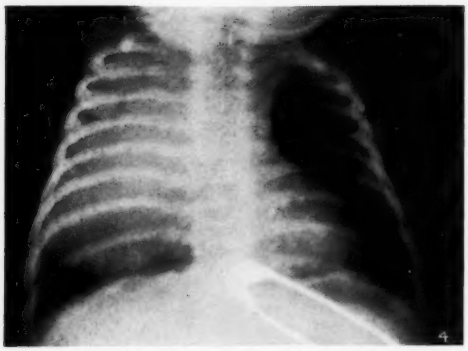

FIG. 4.—Case 4. Distended fluid containing cyst of right upper lobe compressing surrounding lung tissue and displacing superior mediastinum toward the opposite side.

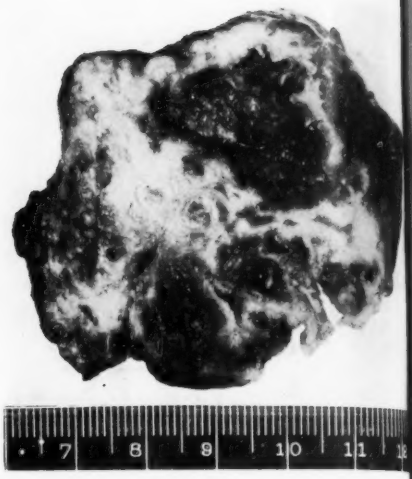

FIG. 5.—Case 4. Cut specimen of right upper lo revealing chronic abscess cavity.

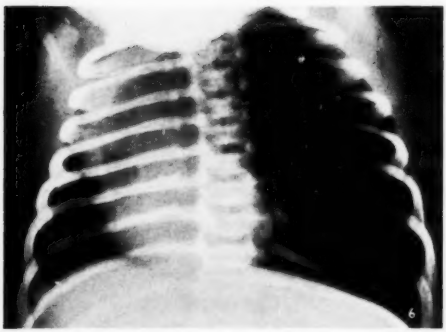

FIG. 6.—Case 5. Obstructive emphysema of the left upper lobe due possibly to congenital atresia of the bronchioles.

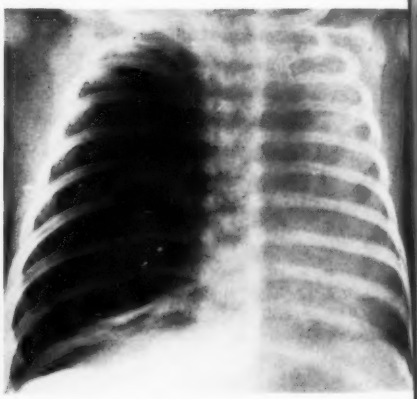

FIG. 7.—Case 6. Obstructive emphysema of th right upper lobe due to congenital atresia of th orifice of the right upper lobe bronchus.

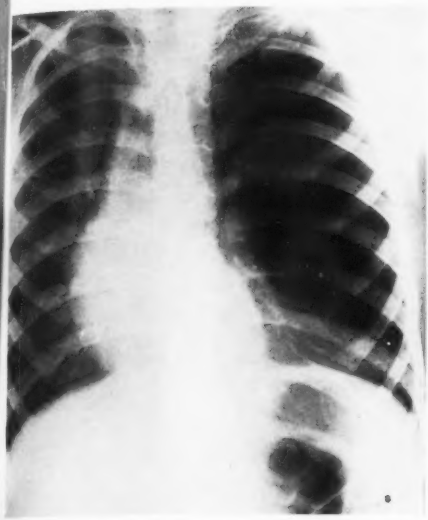

FIG. 8.—Case 7. Obstructive emphysema of left upper lobe.

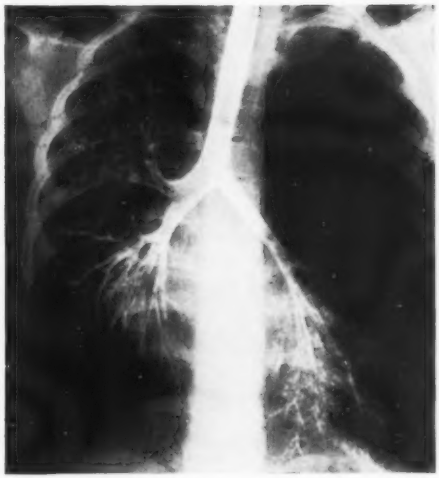

FIG. 9.—Case 7.—Bronchogram revealed no evidence of any upper lobe bronchus or other communication with the bronchial tree.

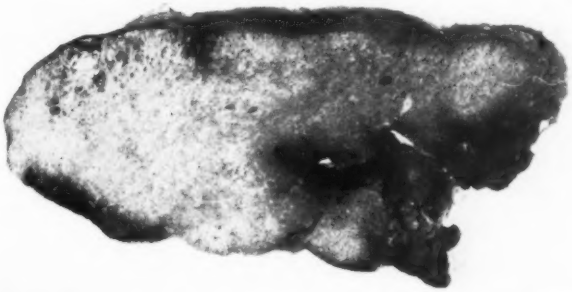

FIG. 10.—Case 7. Cut surface of resected left upper lobe, showing diffuse emphysematous process, with early bulla formation in the apical segment.

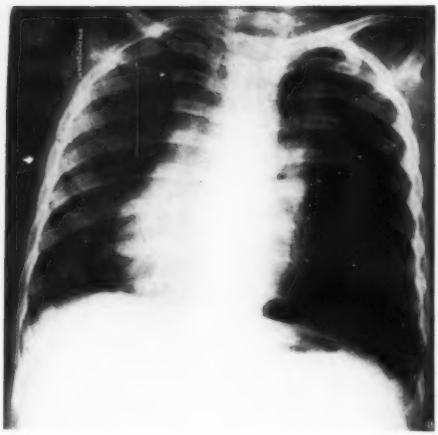

FIG. 11.—Case 8. Obstructive emphysema of left lower lobe due to retained radio-non-opaque foreign body probably present for six months.

21.3.55. Right thoracotomy revealed tension cyst of right lower lobe which was resected. Uneventful convalescence.

Pathologist reported: "Three separate cavities present in right lower lobe; thin, smooth, pale walls lined with thin fibrous tissue with tags of epithelium of bronchial type. Surrounding lung tissue collapsed. Presumably congenital."

Case 3 (Fig. 3, Plate V). S.G. Female, aged 3 years. Liable to frequent colds and bronchitis since infancy; always a poor feeder. X-ray revealed a large cyst occupying the antero-lateral segment of the right upper lobe, but no evidence of any positive tension; fluid level present.

27.3.57. Right thoracotomy revealed a large air-containing cyst which could be "shelled out" from the lobe without sacrificing any normal lung tissue. Several minute bronchial communications oversewn. Convalescence uneventful.

Pathologist reported: "A congenital cyst lined with typical ciliated bronchial epithelium."

This case is included as an example of a congenital cyst which could become a tension cyst at any time with dramatic suddenness and with dangerous sequelæ. Excision was therefore indicated.

Infective Tension Cysts

Pneumatocele

This condition, characterised by the sudden appearance of one or more distended cysts in the lung in the presence of an acute staphylococcal pneumonitis, apparently results from the presence of a ball-valve communication between a bronchus or bronchiole and a localised area of lung necrosis. There is little evidence of suppuration, rarely any fluid in the cyst, and under the influence of chemotherapy the cyst or cysts may disappear as rapidly as they occurred. Surgical treatment is rarely necessary and the degree of tension is insufficient to cause compression of adjacent segments or mediastinal shift. In some cases the cysts persist for many months, long after the disappearance of any signs of active infection, but finally disappear.

Lung abscess

Unless a lung abscess heals promptly under the influence of chemotherapy and postural drainage, the cavity may quickly become lined by bronchial epithelium growing from the orifices of the bronchi communicating with the abscess cavity. Local "healing" is then complete and the cavity may persist as a thin-walled air-containing cyst. According to the size of the bronchial communications a tension build-up can occur at any time when the ball-valve effect becomes operative on normal respiratory bronchial movements. An expanding space-occupying effect may also result from re-infection of the cyst and its distension with inflammatory exudate.

Lung abscesses can occur in infants in the neo-natal period and their rupture into the pleural cavity is probably the commonest cause of tension pneumothorax in the newborn. Many so-called "congenital cysts" of the

lung probably arise as epithelialised neo-natal lung abscesses. It is unusual for the distension to progress to the same degree of severity as in the case of true congenital cysts, probably owing to the restriction imposed by the previous inflammatory changes, and the clinical changes are correspondingly less dramatic. Excision of the lobe or segment containing the cyst is, however, indicated, as at any time the infection can recur and lead to a spill-over infection of adjacent segments.

Case 4 (Fig. 4, Plate VI). C.B. Male, aged 6 weeks. Began to cough at age of two weeks and vomit most feeds. X-ray suggested solid mediastinal tumour or loculated effusion, with displacement of mediastinum to the opposite side.

20.8.54. Right thoracotomy revealed a fluid-containing cyst occupying the right upper lobe and compressing the lower and middle lobes; lobe excised. Uneventful convalescence.

Pathologist reported: "System of intercommunicating cavities full of pus and lined by granulation tissue and scattered areas of bronchial epithelium; no evidence of pre-existing congenital cyst. Pus contained coagulase positive staphylococci." (Fig. 5, Plate VI.)

Obstructive Emphysema

Obstructive emphysema of the newborn is an interesting, rare and dangerous condition. Two of the infants to be described later under this heading would almost certainly have succumbed to suffocation but for prompt surgical treatment. Once the ball-valve effect becomes operative the decline in the infant's respiratory reserve and general condition may be very rapid.

The obstruction results from either congenital atresia of a lobar bronchus at its origin, or from some more generalised malformation in the smaller bronchi or bronchioles of the affected segment. In the one case the cause is obvious; in the other far less so. The macroscopic appearances of the lobe are the same in each case. The lobe is uniformly over-distended, tense, and cannot be emptied by manual pressure at operation. The surface is studded with small emphysematous bullæ tending to coalesce in some areas. Abnormalities of the lobar vascular supply may also be present. Examination of serial sections of specimens fixed in the distended condition have proved disappointing in providing information on the position and nature of the obstruction, unless the observer be blessed with a highly fertile imagination.

Differentiation between obstructive emphysema and a tension pneumothorax is difficult owing to the absence of any radiological lung markings over the emphysematous area. But to differentiate is essential, as needling the chest may produce dramatic relief in the one condition, and aggravate the other by adding a pneumothorax to the embarrassment of the emphysema. It is wiser never to needle unless the diagnosis is certain beyond all reasonable doubt. The cyanosis and dyspnœa are not relieved by oxygen therapy. The infant's condition is too desperate to permit further investigation in the form of bronchoscopy or bronchography to determine the cause of the obstruction, but in an older child the possibility of an intra-bronchial foreign body will have to be ruled out before treatment is planned.

Whether obstructive emphysema of the newborn is a temporary reversible process is not known, and it is certainly not safe to delay surgical treatment in the expectation of spontaneous relief from the tension phenomena.

An exploratory thoracotomy is indicated as an emergency procedure, and as soon as the child is anæsthetised the chest should be opened as rapidly as possible, and widely, to permit relief of tension by delivering the obstructed lobe from the pleural cavity. The diagnosis can then be completed and the lobe, or segment, resected. The remaining, atelectatic, lobes can be readily re-expanded by the anæsthetist except in the case of older children when the atelectasis may have been present for weeks or months.

Case 5 (Fig. 6, Plate VI). R.H. Male, aged 11 days. Asphyxia at birth. Well from second to ninth day. On tenth day refused feeds and became rapidly more cyanosed. Bulging of precordium noted. X-ray (Fig. 6) suggested tension left-sided pneumothorax. Chest needled elsewhere without relief. Further X-rays now suggested a tension cyst of the left lung with a superadded pneumothorax, probably due to the needling. Infant's condition was deteriorating rapidly, so emergency thoracotomy was performed on 17.2.56, revealing a grossly distended and emphysematous left upper lobe which was resected. The anatomy of the pulmonary arterial supply to the lobe was abnormal, the vessels running anterior to the bronchus. Uneventful convalescence.

Pathologist reported: "Obstructive emphysema; dilatation of terminal bronchioles and alveolar ducts; bronchi normal." Further intensive examination of the resected lobe failed to throw any light on the obstruction.

Case 6 (Fig. 7, Plate VI). R.T. Male, aged 6 weeks. Respiration had been difficult since birth. Child referred to the thoracic unit with a diagnosis of "atelectasis of left lung and right lower lobe ? cause." X-ray examination suggested obstructive emphysema of the right upper lobe as no lung trabeculæ were visible in the distended lobe. Bronchoscopy revealed a pin-point orifice of the right upper lobe bronchus but no evidence of any inflammation.

26.11.53. Right thoracotomy revealed obstructive emphysema of the right upper lobe secondary to congenital atresia of the upper lobe bronchus confined to region of its orifice; upper lobe resected. Uneventful convalescence.

Pathologist reported: "Obstructive emphysema and dilatation of bronchioles; branch bronchi normal."

Case 7 (Figs 8 and 9, Plate VII). G.K. Male, aged 6½ years. A relatively fit boy complaining of an unproductive cough for one year. Absent air entry and hyper-resonance over left upper lobe. X-ray suggested obstructive emphysema of left upper lobe. Bronchograms showed no filling of the left upper bronchus and bronchoscopy revealed only a dimple on the lateral wall of the left main bronchus, where the orifice should have been situated.

31.8.56. Left thoracotomy revealed obstructive emphysema of left upper lobe due to atresia of the bronchus and an abnormal arrangement of the pulmonary arteries to the left upper lobe; upper lobe resected. Uneventful convalescence.

Pathologist reported: "Obstructive emphysema of left upper lobe; the bronchus was dilated, but at its proximal end, where it joined the main bronchus,

it was represented by two cartilaginous masses, but no lumen could be detected" (Fig. 10, Plate VII). This case is of interest in that no actual communication with the bronchial tree could be demonstrated and the mode of entry of the air into the obstructed lobe can only be surmised.

Obstructive Emphysema by Foreign Bodies or Post-inflammatory Strictures

This form of pressure or tension phenomenon is unlikely to occur in the newborn infant, but once the infant has developed sufficiently to transfer available foreign bodies to its mouth, then an inhaled foreign body must always be considered as a possible cause of the obstruction responsible for the distension of lobe or lung. Inhaled foreign bodies are seldom revealed by X-ray examination and if any doubt exists a bronchoscopy should be performed under general anæsthesia. If no foreign body is encountered, then a thoracotomy can be proceeded with immediately. It has been the author's practice for some years to bronchoscope every child referred to hospital because the parent suspects such an accident, irrespective of physical signs or radiological appearances. It is surprising how often the examination proves the parents' anxiety to be well founded.

Inflammatory strictures of the bronchus are unlikely to occur in infancy. The rupture of a caseous hilar lymph gland into the bronchial lumen is the usual cause and there may be other evidence of a primary tuberculous lung infection. The diagnosis is confirmed on bronchoscopy and by examination of granulation tissue removed from the area of obstruction. As in the previous case, elimination of the bronchial obstruction produces prompt relief of the tension phenomena in the distal lung tissue.

Case 8 (Fig. 11, Plate VII). R.S. Female, aged 5 years. Chronic non-productive cough and dyspnœa for six months. Diminished air entry over left chest and mediastinal shift to the right. X-ray suggested obstructive emphysema of left lower lobe. Bronchoscopy revealed obstruction of the bronchus of this lobe by a vegetable foreign body—the core of a raspberry—which had almost certainly been present for six months. Rapid recovery following bronchoscopic removal.

Summary

1. Eight cases demonstrating various forms of intra-pulmonary positive pressure phenomena, occurring in infancy and childhood, are presented.

2. Tension developmental cysts and obstructive emphysema due to congenital atresia of a bronchus or bronchioles are not uncommon causes of acute asphyxia during the first few weeks of life.

3. The radiological differentiation between tension cysts, obstructive emphysema and tension pneumothorax is difficult and unreliable.

4. Needling of the chest in these conditions is dangerous.

5. Exploratory thoracotomy and excision of the ballooned segment or lobe may prove a life-saving emergency surgical procedure.

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SUCCESSFUL REMOVAL OF A MYXOMA FROM THE LEFT ATRIUM

By J. R. Belcher

The Middlesex Hospital, London

Successful removal of a myxoma from the left atrium has hitherto been recorded on three occasions: by Crafoord (1955), Scannell and others (1956), and by Chin and Ross (1957). A fourth case is reported here.

Case History

E.A., a woman aged 52, had rheumatic fever when she was 21, but had been well until 1956. In February of that year, and again in August, she had developed "bronchitis" and had an hæmoptysis. After this she had become increasingly dyspnœic, and in February 1957 she had a right pulmonary embolism. By this time she had severe but variable dyspnœa, which was aggravated by lying on the left side.

On examination, the auscultatory signs were not typical of mitral stenosis. The third and auricular sounds were always present, but an opening snap was never heard with certainty. The diastolic murmur varied in intensity and duration, and an apical systolic murmur was also heard occasionally. The first sound at the apex and the pulmonary component of the second sound were very loud. Both the radiograph and the E.C.G. showed evidence of a considerably raised pulmonary vascular resistance.

In view of the history and the signs, a provisional diagnosis of mitral stenosis with high pulmonary vascular resistance was made, and cardiotomy was thought to be essential.

At operation on 5.6.57 (the mean pulmonary artery pressure being 59 cm. of water), the left atrium was reached via a left postero-lateral incision. As soon as the atrium was explored a soft mass was felt arising from the interatrial septum. The mitral valve could not be palpated completely as the mass lay over the anteromedial cusp, but it was apparently normal.

It was decided to remove the tumour without delay. The wound was closed completely, and the patient was then cooled in a bath to 30·6°C. The chest was re-opened through the fourth interspaces. The superior and the inferior venæ cavæ and the great vessels were isolated, and the circulation was stopped. An incision was made into the right atrium and thence into the left atrium through the fossa ovalis. The tumour was encountered immediately as it arose from the septum. As soon as an attempt was made to remove it, it broke up into a number of pieces; these were scooped and sucked out until the atrial cavity was empty (Fig. 1). The atria were then filled with saline and the incisions in the septum and the right atrial wall were sewn. The circulation was restarted, the time of complete arrest having been 9 minutes 45 seconds. The cerebral vessels were occluded for the first few heart beats, and some air was seen in the coronary arteries. Ventricular fibrillation developed and lasted about 20 minutes, but normal rhythm was restored after four or five shocks with the defibrillator and the injection of 1 c.c. 1/1000 adrenalin.

(*Received for publication September* 3, 1957.)

PLATE VIII

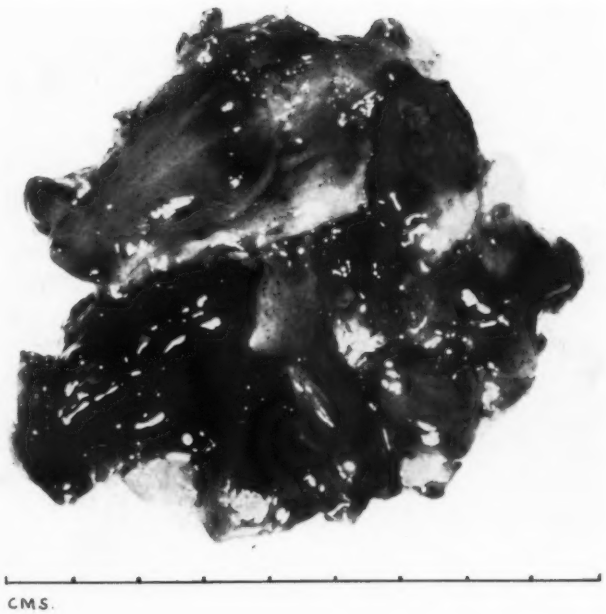

FIG. 1.—A photograph of the tumour mass removed piecemeal.

To face p. 62

After the operation transient jaundice appeared, but this cleared quickly. She then made an uninterrupted recovery. On discharge from hospital her heart sounds were normal and her disability had improved considerably.

Comment

In the majority of cases where myxomata have been encountered at operation it has been an unexpected finding. This has been true both of the unsuccessful cases and the successful ones of Scannell and others (1956), of Chin and Ross (1957), and the one reported here.

In the patient reported by Crafoord (1955) a correct diagnosis was made before the operation by angiocardiography, apparently the only way the diagnosis can be made with certainty.

Crafoord and Scannell removed the tumours through an incision in the left atrial wall; Chin and Ross, following the suggestion of Brock (1956), approached it from the right side through the interatrial septum, and this method was also used in the case reported here. In most of the reports attempts have been made to remove the tumour at a second operation after its accidental discovery, but in the case of Crafoord, as the correct diagnosis had been made, it was possible to remove it in one stage. The known risk of embolism led to the decision to remove the tumour in one stage in the case recorded here.

It is not yet clear whether it is better to use the left or the right atrial approach, but it is certain that removal of the tumours should not be attempted without some form of circulatory arrest. Crafoord used an extra corporeal circulation while hypothermia was used in the other three cases.

Where hypothermia has been employed, Chin and Ross say that a circulatory cooling method offers great advantages, but if the right atrial approach is to be made, it is felt that little if any time was lost by using the safer and simpler surface-cooling method (Sellick, 1957). In the case described here the whole operation was completed in five hours.

Finally, all descriptions of myxomata stress their friability; hence the ever-present risk of embolism. This suggests that the tumours should be removed as soon as they are encountered, and not, if it is at all possible, at a second operation.

Summary

1. A case in which a myxoma was successfully removed from the left atrium is described.

2. The tumour was removed via the right atrium under hypothermia.

3. The diagnosis was not made before the operation, but the tumour was removed through a trans-sternal incision after suture of the original postero-lateral thoracotomy.

My thanks are due to Dr. D. E. Bedford, who referred the case to me.

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SPONTANEOUS PNEUMOTHORAX

By T. F. McCarthy and D. P. Misra

From the Stockport Clinical Area

Spontaneous pneumothorax, although not a very common condition, is nevertheless seen sufficiently often in hospital practice to have been fairly extensively reviewed in the last decade. It is, however, a condition in which the true ætiology often remains in doubt and in which widely differing views as to prognosis are held. These views often depend on whether the cases are being seen as they occur, or are a selected group such as those seen at a special chest centre. The reason for adding to the number of reviews is to describe a small series as it occurred, to suggest a method of management of cases in keeping with the known facts, and to describe the treatment of certain cases by continuous suction, a method which, although it is in use at many centres, we have not previously seen described.

Incidence

Among a population of approximately 389,000 we have been able to trace 28 cases in the records of the two chest clinics, and the two main hospitals of the district, over the last five years.

Age and Sex Distribution

	11-20 *years*	21-30	31-40	41-50	51-60	61+
Males	1	6	6	5	5	1
Females	0	1	2	1	0	0

Thus in all age groups the condition is far less common in women, as has been described elsewhere.

Mode of Onset

Three cases in the series were revealed by mass radiography surveys, or by routine radiography; only one, however, was found to be symptom-free on questioning. One case gave a history of a " clicking " noise on respiration, the only other symptom being a slight shoulder ache. In all other cases the presenting symptoms were pain and breathlessness, the intensity of the pain varying from slight to very severe. The classical picture of sudden onset of pain and dyspnœa, which causes the patient to cease his activities and can be accurately timed, was commonly obtained, but a gradual onset occurred in 10 cases.

(*Received for publication July* 19, 1957.)

Association of Spontaneous Pneumothorax with Tuberculosis

Three cases were associated with active pulmonary tuberculosis. In all, the pneumothorax occurred late in the history of the disease, one being a terminal event in extremely advanced disease.

One of these cases is interesting in that the tuberculosis was associated with hypertrophic emphysema and cyst formation and there were seven recurrences of spontaneous pneumothorax bilateral in distribution, over a period of eleven years.

Association with Other Chest Conditions

No lesion discovered	*Bronchitis and emphysema*	*Emphysema with bullous formation*	*Isolated bleb on surface of collapsed lung*	*Scarring of lung fields*	*Traumatic*
14	4	2	1	3	1

In 14 of the 25 non-tuberculous cases, including 6 of the recurrent cases, no associated chest condition could be found. X-ray examination either during or after the attack often showed nothing to account for it. The commonest associated condition was chronic bronchitis with clinical and radiological evidence of emphysema. The more marked emphysema was found chiefly in the older age groups. One case only showed an isolated bulla on the surface of the collapsed lung and 2 had gross hypertrophic emphysema with apical emphysematous bullæ. Three cases showed scarring of the lung, chiefly apical, as an isolated finding.

The traumatic case was a male aged 63 years who was fibrillating, had an enlarged heart and a right-sided pleural effusion. The pleural fluid withdrawn was found on pathological examination to be a transudate. An electrocardiogram showed evidence of an anterior infarct and a diagnosis of congestive cardiac failure due to myocardial infarction was made. Pericardial paracentesis was carried out twice and 6-8 ounces of fluid were withdrawn on each occasion. On the second occasion the patient developed a bilateral pneumothorax. The right side absorbed uneventfully within a week, but, owing to the patient's distress and dyspnœa, air had to be aspirated from the left side on successive days. Since the lung failed to expand continuous suction through

Recurrent Cases

	Rest or palliative measures	*Aspiration of air*	*Injection of patients' own blood*	*Tube and water seal drainage*	*Tube and continuous suction*	*Decortication*	*Total occurrences*
Non-recurrent: 18 cases ..	9	3	0	0	5	1	18
Recurrent: 7 cases ..	14	1	3	1	2	0	21

an intercostal catheter was instituted and complete expansion obtained, the tube being removed on the fourth day. Routine cardiological treatment was then continued.

Of the 25 non-tuberculous cases in the series, 7 were recurrent, 5 on the same side and 2 on the opposite side; the two latter had no treatment other than rest or palliative measures for either occurrence.

Among the 5 cases with true recurrences—*i.e.*, occurring on the same side—only 2 recurred more than once. One of these cases refused all investigation and treatment other than clinical and radiological examination, the other case recurred five times. There were seven recurrences after rest or palliative measures, two after pleurodesis using the patients' own blood, one after intercostal drainage with a water seal and one after taking off air with a Maxwell pneumothorax apparatus. There was no recurrence after continuous suction with an electric pump using an indwelling intercostal catheter. One case failed to expand with continuous suction and eventually had to be treated by decortication.

Thus in this small series the recurrence rate is higher than the 20 per cent. quoted by Schneider and Reissman (1945), among inducted men in the U.S. Forces. In spite of this, their statement that undue pessimism at the time of the first attack should be avoided and the patient encouraged to return to normal work and activities as soon as possible, would seem to be justified.

Methods of Treatment Used

Cases with a first occurrence of pneumothorax usually attended a chest clinic or hospital out-patient department some days after the incident, often with the symptoms of pain and dyspnœa already lessening. Those in which no cause was apparent were treated as out-patients with rest or symptomatic measures alone, being seen weekly at the chest clinic or out-patient department. As soon as the lung had expanded completely, they were encouraged to resume normal work and activities.

In those cases in which substantial expansion had not taken place within a fortnight more active treatment was instituted. When expansion was not taking place, aspiration of air was tried as in-patient treatment, unless the patient wished to avoid hospital admission. A pneumothorax needle and a Maxwell type of pneumothorax apparatus was used. In recurrent or long-standing cases, although pleurodesis by injection of the patient's own blood had been used in the earlier cases, the method favoured was continuous suction through an indwelling intercostal catheter using an electric pump.

Under local anæsthesia an incision is made in the third intercostal space anteriorly. A size 24 French gauge Nelson's empyema trocar and cannula is inserted and a size 22 F.G. soft rubber catheter introduced through the cannula into the pleural space for a distance of a few inches, preferably lying in an upward direction. The catheter is then secured to the skin with sutures. It is then connected to an electric pump and continuous suction of 10-15 cm. of water is applied. After forty-eight hours the patient is X-rayed and if the

lung is in contact with the chest wall the tube is clipped off. The patient is X-rayed daily for the next two days and if the lung remains fully expanded the tube is removed. Should the lung not be fully expanded after the initial forty-eight hours, or should there be a recurrence, then further suction is applied. If the lung is not fully expanded within four days further investigation must be carried out.

In only one case in the series was expansion not obtained and this case later needed decortication to obtain expansion of the lung. It was suggested that intermittent suction might improve the results and this was tried as twenty minutes in each hour in some of the later cases in the series. There would seem to be very little difference in the results. A small quantity of fluid occasionally developed, but this has not been a troublesome complication and aspiration has seldom been needed. Antibiotics have not been used as a routine, but should pyrexia or other evidence of infection develop, they could be used both locally and systemically. Few patients complained of discomfort and little sedation has been necessary.

A typical case and the case which required decortication are described:

A business executive, aged 48 years, was seen in the out-patient department three weeks after the sudden onset of right-sided chest pain and dyspnœa. There was no previous history of chest trouble. The pain, which occurred while walking, soon settled and the dyspnœa improved but did not entirely disappear. There was no cough or sputum. A clinical diagnosis of a right-sided pneumothorax was made and confirmed radiologically. Hospital admission was suggested to the patient, but owing to the mildness of his symptoms and his business and domestic situation, he wished to avoid this and he was asked to return in two weeks. His condition showed little change, but since he remained unwilling to be admitted to hospital he was retained under observation as an out-patient. Two thousand ml. of air were aspirated from the right side of his chest on two occasions without producing permanent expansion of the lung.

The patient was finally persuaded to enter hospital, and suction through an intercostal catheter by the method described was instituted 108 days after the occurrence of the pneumothorax. The lung expanded completely and when it had remained so for a few days the tube was removed. A little fluid accumulated at the right base, but this did not require aspiration. Antibiotics were not used in this case and the only sedative required was small doses of a barbiturate at night. The period of hospitalisation was fourteen days and the patient returned to work after a holiday lasting a fortnight.

The case which required decortication was a male clerk, aged 35 years. He gave a past history of left-sided pleural pain of short duration eight and a half years previously, but he was not X-rayed at that time. Five years previously he was seen at the chest clinic following cough and vague chest pain of a month's duration. A shallow left-sided pneumothorax was found, which expanded uneventfully without treatment. He was kept under observation, however, for four years.

After being in bed for a week undergoing treatment from his doctor for pain in the lumbar region, he experienced severe chest pain of sudden onset,

and became distressed and collapsed. He was admitted to hospital as an emergency and physical signs of a left-sided pneumothorax under high tension were found. Radiologically there was complete collapse of the left lung with displacement of the trachea and mediastinum to the right. After aspiration of 2,000 ml. of air the patient became more comfortable, but the X-ray showed little change. Three days later a further 8,000 ml. of air were removed, but X-ray the next morning still showed an almost completely collapsed lung. Continuous suction through an intercostal catheter was started, systemic penicillin being given prophylactically. The lung, however, had failed to expand after forty-eight hours, although the patient's clinical condition had improved, and it was therefore decided to continue suction for a further forty-eight hours. At the end of this period a mediastinal shift was still present and fluid was accumulating in the pleural space, eventually reaching the level of the second intercostal space. The fluid was sterile on culture.

The patient was transferred to the Regional Thoracic Surgical Unit for further investigation. Here continuous suction was again employed and considerable expansion was obtained, but it was not complete. Decortication was later carried out and a very thick pleura was encountered with straw-coloured fluid and lumps of fibrin. Progress was satisfactory, but a lateral X-ray ten days later showed the presence of an anterior air space. Continuous suction was again applied and some further expansion was obtained, but a small space remained which could not be obliterated.

Since discharge from hospital the patient has remained very well and is carrying out his normal work. At his last review six months after decortication the residual air space had practically disappeared.

Follow-up of Cases

0-6 *months*	7-12 *months*	1-2 *years*
1	1	5

The follow-up period is short, but there have as yet been no recurrences following continuous suction with an intercostal catheter.

Hospitalisation

With the exception of the traumatic case already described, which required further treatment in the general wards for the heart condition, and the case which required decortication (hospitalisation sixty-seven days), it was found possible to discharge all cases within a fortnight of the institution of continuous suction. Patients were allowed up the day after removal of the tube and usually discharged a few days later. Instructions were given that they should return to normal work and activities as soon as possible and always within a fortnight.

This compares favourably with other methods of treatment where the period of hospitalisation has varied between six days in a case treated by rest alone and eighty-seven days in one which was later treated by continuous suction and discharged routinely. The saving of hospital time and the speedy return of patients to work is thus one of the major features of the method.

Discussion

Various methods of obtaining pleural symphysis have been described by different authors. A number of agents have been used, including silver nitrate (Brock, 1948), iodised oil (Hennell and Steinburg, 1949), kaolin (Maxwell, 1954), and others. Kreutzer *et al.* (1952) reported the advantages of the addition of suction using an indwelling catheter, suggesting that the mechanical trauma of the tube assisted pleural symphysis once the lung had expanded. Maxwell (1954) suggested that suction to expand the lung might be the most important element in treatment, as pleural fusion occurred in a few days as compared with a few weeks if kaolin was injected without suction.

This series seems to bear out these suggestions, as although no pleural irritant was used symphysis was obtained in all cases except one. In consequence, although the period of hospitalisation was of similar duration and the return to work as speedy, very little pain and discomfort were caused by the procedure as the use of a pleural irritant was avoided.

Summary

A series of 28 cases of spontaneous pneumothorax occurring over the last five years has been described and discussed. A method of treatment, which has been comfortable for the patient, has saved hospital time and given satisfactory results, is described.

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THE ASSOCIATION OF SARCOIDOSIS, ACTIVE PULMONARY TUBERCULOSIS AND INSENSITIVITY TO TUBERCULIN

By A. J. Taylor

From the Southampton Chest Hospital

Sarcoidosis and tuberculosis may occur in the same patient, but it is uncommon for the tuberculosis to be in an active caseating phase (Scadding, 1956a). Active pulmonary tuberculosis with low skin sensitivity may also occur and sometimes resembles sarcoidosis (Scadding, 1956b).

The first case to be described is that of a woman who developed sarcoidosis and active pulmonary tuberculosis five years after tuberculous peritonitis; the second case is that of a man who was thought to have sarcoidosis before tubercle bacilli were cultured from his sputum.

Case 1. W.M., a 42-year-old housewife, in 1949 complained of loss of weight and abdominal swelling, and was found at a laparotomy to have tuberculous peritonitis. She was treated with streptomycin and was well until 1952 when she developed a productive cough. In June 1953, during an attack of right-sided pleurisy, tubercle bacilli were cultured from her sputum, and her chest radiograph (Fig. 1) was abnormal, with scattered shadows throughout both lung fields, an enlarged hilar shadow on the right where the costophrenic angle was obliterated, a shadow indicating a 2 cm. cavity in the left upper lobe, and a homogeneous apical opacity. She was admitted to a sanatorium: the positive sputum finding was confirmed and she was found to be insensitive to 1/100 old tuberculin. For six months she was treated with intramuscular streptomycin 1 g. three times a week (to a total of 84 g.), PAS 12 g. daily and isoniazid 300 mg. daily. Her sputum became negative and she felt well, but there was no radiological evidence of improvement. She was discharged home in June 1954. In February 1955 her sputum again contained *M. tuberculosis*, which was cultured but not inoculated into a guinea-pig. She was readmitted to the sanatorium and was found to have dull red plaques in the skin of her right upper arm and forearm and left upper arm; she was still insensitive to 1/100 old tuberculin and the radiograph was much as it had been one year earlier.

She was treated with streptomycin, PAS and isoniazid in the same doses as before for five months, then, on account of depressive psychosis, was transferred to a Mental Hospital.

On 10.1.56 she had a small hæmoptysis and was transferred to this hospital; her only other symptom was dyspnœa. The abnormalities found on examination were a poor general condition, poor chest expansion, impaired percussion note and bronchial breath sounds over the left upper zone posteriorly, and the

(*Received for publication September* 9, 1957.)

PLATE IX

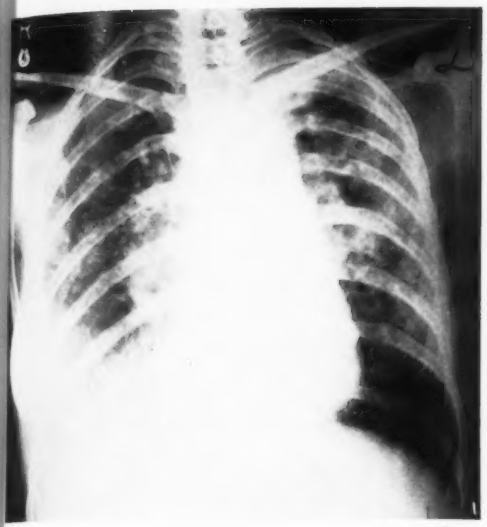

FIG. 1

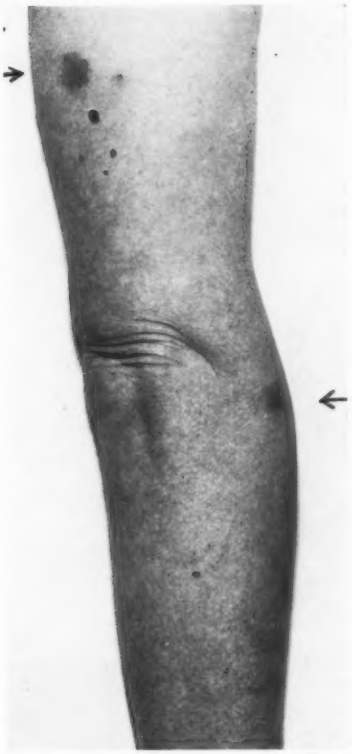

FIG. 2

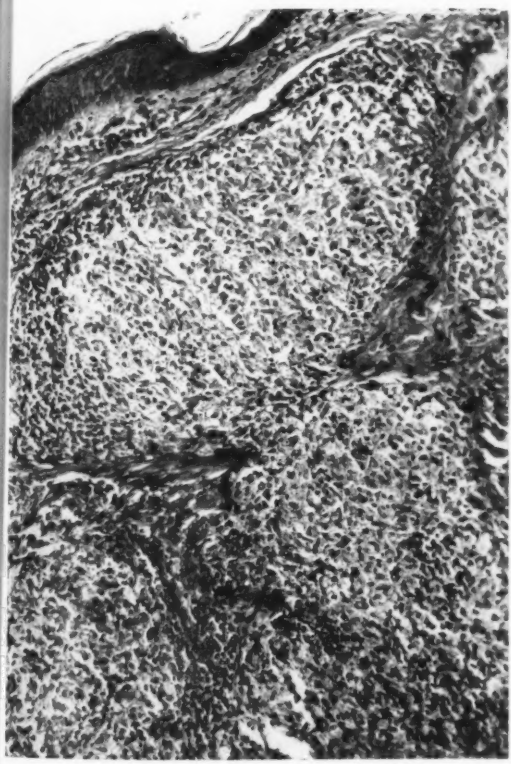

FIG. 3

FIG. 1.—June 1953—radiograph with shadowing throughout both lung fields, enlargement of the right hilar shadow, and obliteration of the right costophrenic angle. Shadowing in the left second intercostal space represents a cavity in the left upper lobe.

FIG. 2.—Photograph showing the skin lesions in the right arm in January 1956. The sarcoid lesions are indicated by arrows.

FIG. 3.—Microphotograph of a biopsy from one of the sarcoid skin lesions. (×135).

To face p. 70

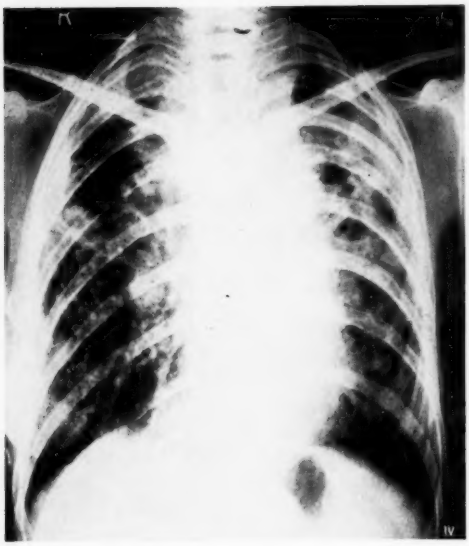

FIG. 4.—Radiograph in August 1956, showing increased shadowing in the right upper zone and a large left apical cavity.

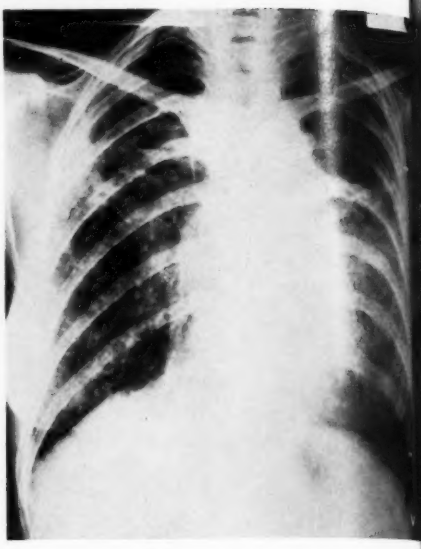

FIG. 5.—Radiograph showing bilateral apical cavitation and persistent shadowing throughout both lung fields.

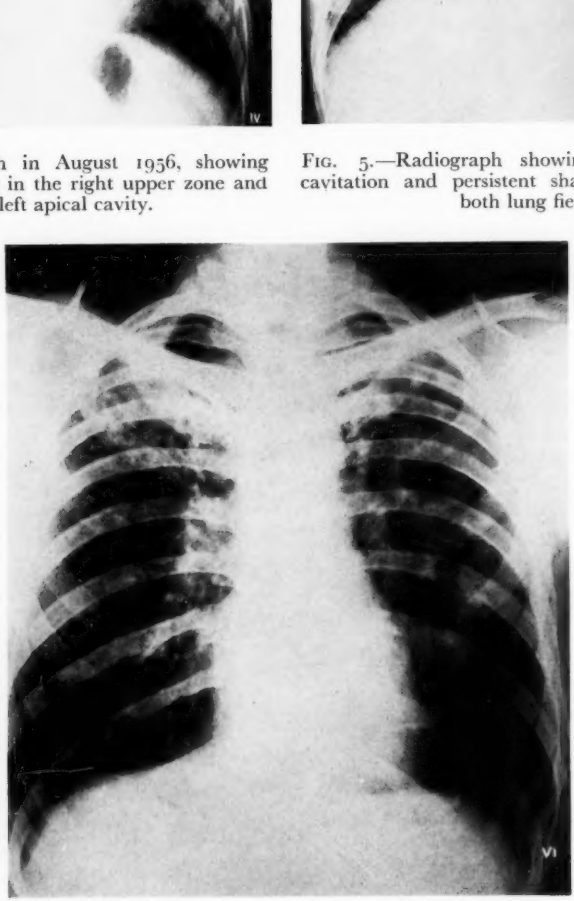

FIG. 6.—Radiograph in January 1954, with shadowing throughout both lung fields.

skin lesions from ¼-1 inch in diameter, scattered about on the arms. Some were uniform in consistency and others were made up of aggregates of papules; the colour varied from a deep purplish-red in the larger lesions to a brownish-red in the more papular lesions (Fig. 2). Her B.P. was 120/70.

The blood picture was normal. The serum protein content was 6·2 g./100 ml. (A/G=0·83/1); the E.S.R. (Westergren) was 67 mm. in the first hour, and electrophoresis showed that there was a diffuse increase of gamma globulin. The serum calcium was not raised. The Mantoux was negative (1/10 O.T.) and the radiograph was the same as it had been one year before.

Biopsies from two of the skin lesions gave a histological picture (Fig. 3), said to be quite typical of sarcoidosis. The corium was infiltrated by sheets of epithelioid cells, arranged in several areas in a follicular pattern, with a few scattered aggregations of giant cells but no evidence of caseation.

Treatment with calciferol 100,000 units daily, streptomycin, PAS and isoniazid was stopped after two weeks because of repeated vomiting. The blood urea (61 mg./100 ml.) and serum calcium (14·4 mg./100 ml.) which were raised, and the urine which contained moderate numbers of granular casts, returned to normal.

In August 1956 she began to lose weight. Although the right lower zone was clearer there was radiological evidence of deterioration in her lung condition with a cavity in the left apex (Fig. 4), and tubercle bacilli were again grown from her sputum.

Streptomycin (1 g. thrice weekly) and daily PAS (12 g.) and isoniazid (300 mg.) were again given, but nausea and vomiting recurred and the drugs had to be stopped. Her blood pressure had risen to 180/100, and the blood urea was 113 mg./100 ml. The Hb. had fallen to 9·9 g./100 ml. The Mantoux test was now found to be positive with 1/1,000 old tuberculin.

In the next two months the skin lesions gradually disappeared and by mid-October her skin was normal.

Nausea and vomiting continued intermittently and she was found to have a gastric ulcer, which responded to treatment.

She was then desensitised to streptomycin which has been given daily (¾ g.) with isoniazid (300 mg.) for eight months.

At present her only symptom is dyspnœa; the only abnormalities on physical examination are related to her chest; the radiograph (Fig. 5) suggests that there is now extensive fibrosis in both lungs, with cavities in both upper lobes. The mediastinal lymph nodes are presumably still enlarged. There is still evidence of renal damage, the blood urea is 76 mg./100 ml. and the urine specific gravity range is only 1·008 to 1·012.

Calciferol may, when used to treat patients with sarcoidosis in particular, cause elevated serum calcium and consequent renal damage. This may be combated by giving cortisone, not given in this instance because of the previous history of mental abnormality. It must be assumed now that the renal function is permanently impaired.

The tuberculin sensitivity is again very low, a minimal reaction being obtained with 1/10 old tuberculin. Treatment with ¾ g. streptomycin and 300 mg. isoniazid daily is being continued.

Case 2. L.F., a male aged 42. A fitter, not exposed to undue hazard from dust, gave a history in 1949 of persistent cough, occasional wheezing and winter bronchitis for eight years. There were no notable findings on physical exam-

ination, but his radiograph was abnormal with enlarged hilar shadows, and a generalised increase in lung markings.

His symptoms continued, and a few months before he went for a mass radiograph in December 1953 he began to have vague chest pains, and his cough became productive of small amounts of purulent sputum. The radiograph had fine and coarse shadows scattered throughout both lung fields (Fig. 6). Physical examination was largely negative. A Mantoux test using 1/100 O.T. was reported negative and sputum specimens were negative on microscopic examination for *M. tuberculosis* (but later positive on culture). A liver biopsy was negative for sarcoidosis, but the clinical evidence was thought to be in favour of that diagnosis.

The patient was treated with streptomycin (1 g. daily) and PAS (15 g. daily). Three months later tubercle bacilli, pathogenic to a guinea-pig, were cultured from gastric lavage material, a Mantoux test with 1/10 O.T. was negative, and the radiographic shadows had cleared to a large extent.

Treatment with streptomycin and PAS was continued for forty weeks. Then the patient felt well and his radiograph was scarcely abnormal. A Mantoux test was still negative using 1/10 O.T. Gastric lavage had given repeatedly negative results.

He was allowed to restart work early in 1956 and has remained well since.

Discussion

These two patients present two different aspects of the problem of active pulmonary tuberculosis with insensitivity to tuberculin.

There is no doubt that the first patient had generalised sarcoidosis. Typical sarcoid histological changes were seen in her skin biopsy; her hilar lymph nodes were enlarged; there were fine scattered shadows in both lung fields, and she had hyperglobulinæmia.

There is also no doubt that she had active cavitating pulmonary tuberculosis. Tubercle bacilli were cultured from her sputum on four separate occasions and there was definite evidence of pleural involvement and upper lobe cavitation which are not described as occurring in sarcoidosis (Simon, 1957; Shanks and Kerley, 1950/1).

There is a frequently recognised association between sarcoidosis and tuberculosis, although no cultural or immunological technique has proved a direct relationship (Leitner, 1949; Longcope and Freiman, 1952). Scadding (1956a) and Mather, Dawson and Hoyle (1955) believe there is frequently a direct ætiological relationship. None the less it is uncommon to find evidence of sarcoidosis and active cavitating pulmonary tuberculosis together.

Cowdell (1954), in reviewing 94 cases of sarcoidosis, found only 1 associated with pulmonary tuberculosis, and, of the 14 patients of 142 with sarcoidosis in whom tubercle bacilli were found, Scadding (1956a) reported that in only 3 was the finding associated with a frankly caseating phase and the development of tuberculin sensitivity. Ten others were still in the sarcoid phase and no clinical or radiological change was detected.

Mascher (1951) states that when tuberculosis complicates sarcoidosis tuberculin sensitivity returns, and this view is confirmed by Scadding's series

of 14 patients of whom the three who developed caseating tuberculosis became sensitive to tuberculin, whereas the Mantoux test remained negative to 100 T.U. in 8; to 10 T.U. in 1; and positive to 10 T.U. in one of the group who remained in the sarcoid phase when tubercle bacilli were found. The patient, W.M., remained negative to 1/100 old tuberculin even when her sputum was positive and her lung cavitated. It was not until her skin lesions had healed some months later, and then only for a short time, that she gave a positive reaction to 1/1,000 old tuberculin; this was soon after radiological evidence had suggested spread of tuberculosis in her left lung. It is not known whether or not the tuberculin sensitivity which was absent six months before returned prior to the spread of disease in August 1956.

The second patient, before tubercle bacilli were cultured and a negative biopsy had been obtained, was thought to have sarcoidosis. Then a diagnosis of active pulmonary tuberculosis with low, or absent, tuberculin sensitivity was made. Hedvall (1943), Mascher (1951) and Scadding (1956b) have each reported several cases with active pulmonary tuberculosis and low tuberculin sensitivity. Scadding (1956b) described the disease in his four cases not reacting to 100 T.U. as indolent, and noted that that type of disease responded poorly to antibacterial treatment. This second case history shows that low tuberculin sensitivity is not necessarily related to a poor response to antibacterial drugs, as there was obvious improvement, as shown by radiographs, after chemotherapy for three months.

Had she not developed sarcoid skin lesions the first patient could have been included in this group, which, according to Scadding, includes cases not distinct from some cases of sarcoidosis.

Summary

The case histories of two patients in whom tuberculin sensitivity was low and from whose secretions tubercle bacilli were cultured are described and discussed.

My thanks are due to Dr. W. M. Macleod for permission to publish these two cases and for helpful criticism, to Dr. R. A. Goodbody for the pathological description, and to Mr. M. H. Travers for the photographs.

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TOMOGRAPHIC BRONCHOGRAPHY IN THE INVESTIGATION OF PULMONARY TUBERCULOSIS

By R. Y. Keers* and A. R. Adams*

From the Deeside Sanatoria, Aberdeenshire

Two major contra-indications to the investigation of pulmonary tuberculosis by means of bronchography have been eliminated by the events of recent years. The disadvantages of prolonged alteration in the radiographic appearances, due to the retention of radio-opaque material in the alveoli, have been banished by the introduction of propyliodone, with its power of rapid absorption, while the dangers of exacerbation of an active focus or of bronchogenic dissemination have been reduced to negligible proportions by the concurrent administration of adequate anti-tuberculous chemotherapy.

Publications recording the safety of bronchography in pulmonary tuberculosis under these new conditions have been accompanied by reports dealing with its practical advantages and the value of the additional information which it provides. Shaw *et al.* (1954), reporting a series of 100 patients in whom bronchography was performed prior to resection surgery, found this examination most helpful in defining accurately the segmental localisation of disease, and considered that in this respect it was superior to all other radiographic procedures. They commented on the frequency with which abnormalities of the bronchial tree were discovered in association with lesions previously believed to involve only the parenchyma. Forgacs (1955), reviewing a series of 120 cases, agrees with Shaw and his colleagues that the main use of bronchography in pulmonary tuberculosis is in the pre-operative planning of resection procedures. He considers that, once the diagnosis has been established, bronchography contributes little to a fuller understanding of the disease, as the bronchi draining tuberculous cavities are usually too small to be studied bronchographically, and on those occasions when they may be demonstrated accidentally they tend to be lost in a network of superimposed shadows. For the same reason he has found the study of tuberculosis spreading along the submucosal lymphatic channels to be unrewarding.

It seemed reasonable to suggest that tomography, which had provided an invaluable supplement to standard radiography, might with advantage be incorporated into bronchographic examination in the hope that it would permit more detailed study of individual bronchial divisions and, in particular, those divisions in direct anatomical relationship with parenchymal foci. Few references to this method of examination—tomobronchography—have yet appeared in the literature. Chadbourne *et al.* (1954) have recorded briefly

* Now at Cheshire Joint Sanatorium, Market Drayton, Salop.

(*Received for publication August* 7, 1957.)

their experience with tomobronchography, which they have found particularly valuable in cases where interpretation of the conventional bronchogram is likely to be difficult as a result of extensive pathological changes in the lung parenchyma. They consider it specially helpful in studying the axillary branches and feel that, with its aid, an accurate anatomical plan of the bronchial divisions, as well as of the pulmonary lesions, can be mapped out. They also comment on its value in cases where some of the contrast medium has entered the opposite bronchial tree, when lateral tomobronchograms enable this to be dissociated from the side under review. Zsebök (1956) considers that tomobronchography is an essential part of bronchographic examination, and supports his view with illustrations demonstrating by this method bronchial abnormalities which were not apparent on standard bronchograms.

Material

During the past two years we have endeavoured to determine the value of this method of examination in the pre-operative assessment of cases of pulmonary tuberculosis. Bronchography was already part of our routine investigation of such cases and it was, therefore, relatively simple to arrange for tomography to be carried out while the opaque medium was still in the bronchial tree.

In the course of the study 218 sets of tomobronchograms were obtained during 171 bronchographic examinations, and recently these films have been reviewed. The purpose of the review was (1) to decide in what proportion of the cases tomobronchography had provided information additional to that obtained from standard bronchograms; (2) to establish criteria which would enable us in future to select the cases in which tomobronchography was likely to prove most profitable.

Technique

All patients included in this series were suffering from pulmonary tuberculosis and all were on one of the standard chemotherapeutic régimes at the time bronchography was carried out. Consequently, the majority had become sputum negative before examination, although we did not regard a positive sputum as a contra-indication to bronchography, provided the bacilli were known to be sensitive to the drugs employed. Few of the patients investigated had more than half a fluid ounce of sputum daily and preliminary postural drainage was only rarely required. Postural coughing after completion of bronchography was carried out in all cases.

The only premedication used was one of the rapidly acting barbiturates which has helped to allay apprehension and has reduced vasovagal incidents to a minimum.

The cricothyroid method has been used, for we have found it to be less time consuming and, therefore, less of an ordeal for the patient than over-the-tongue or catheter methods. Occasionally we have seen surgical emphysema as a sequel, but this has always been limited and has caused little discomfort to the patient.

The patient is positioned on an X-ray tilting table with a firm pillow under the shoulders to extend the neck. After preliminary cleaning of the skin a wheal is raised over the cricothyroid membrane with 2 per cent. Xylocaine, using a fine needle. A stronger needle is then substituted and 4-5 c.c. are injected into the trachea via the cricothyroid membrane, the table having been tilted foot down to about 15°. The first 1-2 c.c. injected cause a paroxysm of coughing, but this quickly settles and the remainder can be injected without further reaction.

A small trocar and cannula with a Labat bayonet fitting is introduced through skin and cricothyroid membrane into the trachea. When the trocar is removed air can be heard passing through the cannula if the cannula is in the correct position. A sandbag is then placed under the contralateral shoulder and the filled syringe containing 16-20 c.c. of Dionosil oily is connected. Injection is carried out fairly rapidly with the patient taking long, regular breaths.

On completion of injection, the cannula is withdrawn and the patient turned almost to the prone position and left for three minutes to allow middle lobe or lingula to fill. Upper lobe filling is then obtained by tilting the table head down to 45° and positioning the patient for three minutes almost prone, followed by three minutes almost supine, when filling is usually complete. The patient is screened and further posturing carried out if required, following which postero-anterior, lateral and oblique films are taken, followed by tomography. The patient is then returned to bed and postural coughing enforced.

Without tomography the process can be unhurriedly completed by a trained team in 20 minutes and with tomography in 30 to 35 minutes.

Analysis of Material and Results

A careful review of the 218 sets of tomobronchograms and their accompanying standard bronchograms showed that in thirty-three instances (15 per cent.) tomographic bronchography had provided information which was not available from bronchography alone. The 218 sets comprised 131 taken in the antero-posterior position and 87 in the lateral position. The analysis was carried a stage further by considering these separately, and it was found that most help had been obtained from the lateral views which had yielded additional information in 19 cases (21 per cent.) as against 14 cases (11 per cent.) in the antero-posterior group.

Table I contains details of this additional information which it was felt had contributed to a fuller understanding of the disease and had influenced therapeutic planning in the 33 cases. Study of these cases showed that the particular situations in which tomobronchography had proved helpful fell into four fairly distinct groups:

(1) *The demonstration of localised abnormalities of limited extent, particularly those occurring in subsegmental divisions.* In all our bronchograms we have aimed at producing radio-opacity of the bronchial tree to bronchiolar level. While

TABLE I.—DETAILS OF ABNORMALITIES FOUND BY TOMOGRAPHIC BRONCHOGRAPHY

Case No.	*Side*	*Type of tomogram*	*Anatomical distribution*	*Details*
G.479	R.	Lat.	Apical segment of lower lobe	Irregular mucosal outline indicating previous disease.
G.495	L.	Lat.	Anterior segment of upper lobe	Stenosis of segmental bronchus and its relation to a solid lesion.
G.500	R.	Lat.	Posterior segment of upper lobe	Filled cavity with irregularity of mucosal outline in its draining bronchus.
G.514	R.	A.P.	Upper lobe	Filled cavity with irregularity of mucosal outline in draining bronchus, also stenosis of adjacent bronchus.
G.519	R.	A.P.	Sub-apical segment of lower lobe	Rat-tailed stenosis of bronchus.
G.551	L.	A.P.	Upper lobe	Filled cavity with irregularity of mucosal outline in its draining bronchus.
G.561	R.	Lat.	Upper lobe	Minor ectatic changes.
G.625	R.	A.P.	Apical segment of lower lobe	Ectasis and stenosis of segmental bronchi.
G.631	L.	A.P.	Apico-post. segment of upper lobe	Rat-tailed bronchial stenosis.
G.642	R.	A.P.	Upper lobe	Solid focus with irregularity of mucosal outline in its related bronchus.
G.643	L.	Lat.	Upper lobe	Filled cavity with detail of its related bronchus.
G.652	L.	A.P.	Upper lobe	Bronchial stenosis, also stenosis of bronchus associated with large (unfilled) cavity.
G.673	L.	A.P.	Upper lobe	Stenosis of bronchus associated with a solid lesion.
G.653	L.	Lat.	Lower lobe	(i) Irregularity of mucosal outline in apical segmental bronchus. (ii) Stenosis of bronchus in sub-apical segment related to an unfilled cavity.
G.358	L.	A.P.	Upper lobe	Rat-tailed stenosis of bronchus with its relation to a solid focus.
G.716	R.	A.P.	Middle lobe	Stenosis of upper branch of middle lobe bronchus.
T.2248	L.	Lat.	Lateral basic segment of lower lobe	(i) Localised bronchiectasis. (ii) Stenosis of bronchus associated with small solid focus.
T.2253	R.	Lat.	Sub-apical segment of lower lobe	Stenosis of otherwise normal segmental bronchus.
T.2262	R.	Lat.	Apical segment of lower lobe	Stenosis of segmental bronchus.
T.2268	L.	Lat.	Upper lobe	Filled cavity with detail of its draining bronchus.
T.2274	L.	A.P.	Apico-post. segment of upper lobe	Stenosis of segmental bronchus associated with a solid lesion.
T.2275	R.	A.P.	Apical segment of lower lobe	Localised bronchiectasis.
T.2277	R.	A.P.	(1) Anterior segment of upper lobe	Stenosis of segmental bronchus.
			(ii) Apical segment of lower lobe	Stenosis of segmental bronchus and its relation to associated solid lesion.

TABLE 1.—*Continued*

Case No.	*Side*	*Type of tomogram*	*Anatomical distribution*	*Details*
T.2287	R.	Lat.	(i) Posterior segment of upper lobe (ii) Anterior segment of upper lobe	(i) Ectasis of segmental bronchus. (ii) Stenosis of branch of segmental bronchus.
T.2289	L.	Lat.	Apical segment of lower lobe	(i) Stenosis of upper branch of segmental bronchus. (ii) Ectasis of lower branch of segmental bronchus.
T.2292	L.	Lat.		Tomograms allowed differentiation to be made between ipsi and contra lateral filling.
T.2299	R.	Lat.	Apical segment of lower lobe	Stenosis of branches of segmental bronchus.
T.2303	R.	Lat.	Lower lobe	Irregularity of mucosal outlines in apical and subapical segmental bronchi.
T.2311	L.	Lat.	Posterior basic segment of lower lobe	Ectasis of branches of segmental bronchus.
T.2329	L.	Lat.	Apico-post. segment of upper lobe	Detail of filled cavity and of mucosal irregularity in its draining bronchus.
T.2334	R.	Lat.	Posterior segment of upper lobe	Rat-tailed stenosis of segmental bronchus.
T.2339	L.	A.P.	Apico-post. segment of upper lobe	Minor ectasis of segmental bronchi.
T.2373	L.	Lat.	Hilar region	Differentiation of grossly distorted and crowded bronchi.

this is a more elaborate filling than that required to demonstrate merely the anatomical distribution of the main parenchymal foci, we have felt it to be necessary, since lack of filling of the peripheral bronchi or bronchioles in an otherwise satisfactory bronchogram may be of clinical significance. In the conventional bronchogram, however, bronchiolar filling may result in minor abnormalities of the smaller bronchi being obscured or overlooked. Instances of such minor abnormalities are (*a*) irregularity of the bronchial wall presenting as a beaded or " goffered " appearance, (*b*) small areas of saccular or cylindrical bronchiectasis (Figs. 1A and 1B), (*c*) bronchial occlusion of either the rat-tailed or rectangular type. These changes may be found in areas which otherwise appear radiologically normal, particularly if the patient has had a prolonged course of chemotherapy, and they form reliable evidence of the involvement of the particular division in the original pathological process. While some of the appearances mentioned are quite compatible with healing of the disease, the information is still of value as an indication of the amount of pulmonary tissue which has suffered some degree of functional impairment. In well-filled bronchograms we have found tomobronchography to be of great value in demonstrating clearly and unmistakably these distal and relatively limited abnormalities.

(2) *The clarification of bronchial anatomy in a lung which has been grossly diseased,*

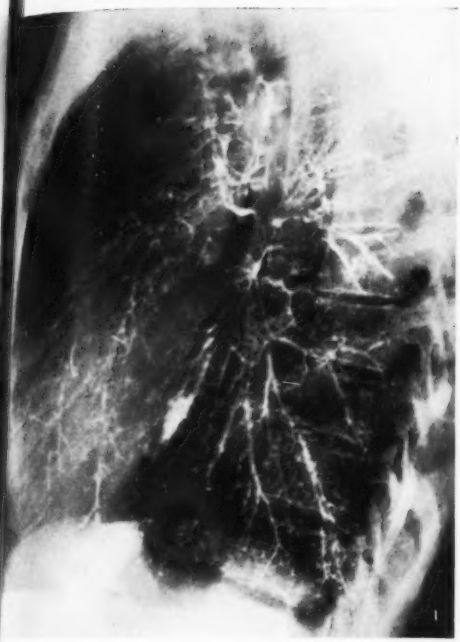

FIG. 1a.—Female, *aet.* 45. Cavitated disease left upper lobe. Left lateral bronchogram shows abnormality of anterior basal division of left lower lobe.

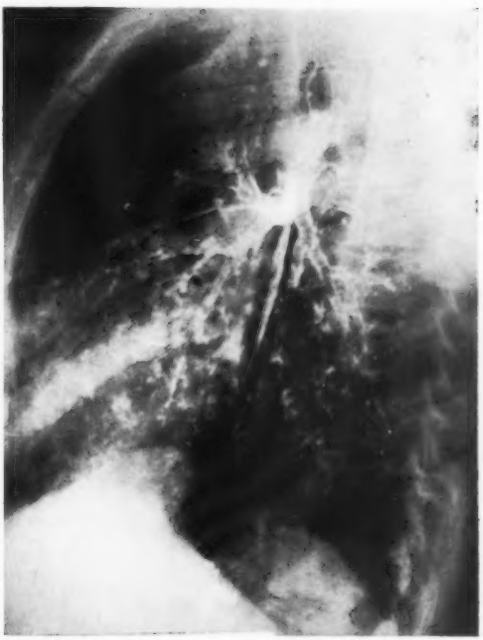

FIG. 2a.—Female, *aet.* 34. Extensive disease of left lung of several years duration, with upper lobe atelectasis. On lateral bronchogram the short thickened division apparently arising from stem bronchus opposite lingular division was incorrectly identified as apical bronchus of lower lobe.

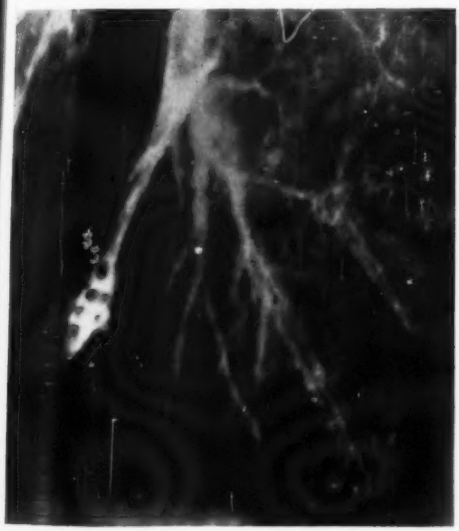

FIG. 1b.—Left lateral tomobronchogram shows abnormality to be a limited area of saccular bronchiectasis.

FIG. 2b.—Lateral tomobronchogram showing supposed lower lobe apical division to be a much distorted and displaced posterior basal bronchus. This interpretation was confirmed at operation.

To face p. 78

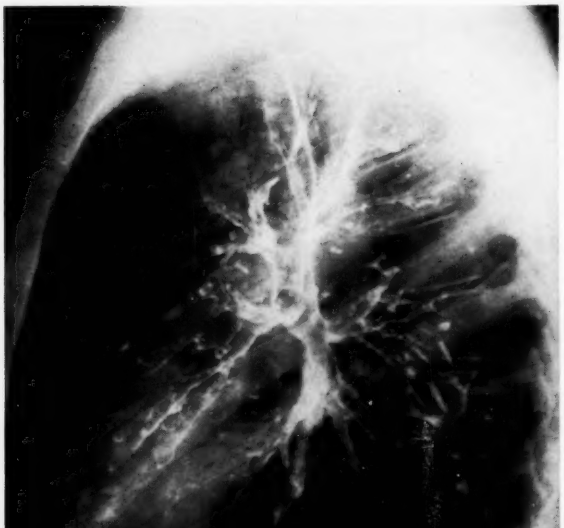

FIG. 3a.—Male, *aet.* 28. Seven years history of bilateral disease. Admitted because of new and persistent cavity in sub-apical segment left lower lobe. Lateral bronchogram after prolonged chemotherapy shows many abnormalities of bronchial sub-divisions.

FIG. 3b.—Lateral tomobronchogram showing cavity and associated bronchus. Medium held up at bronchocavity junction where bronchial lumen appears dilated rather than narrowed. Interpreted as indicative of active endobronchial lesion and confirmed at examination of resected specimen.

Other types of abnormal bronchial "endings" mentioned in the text also seen in this illustration.

or which has been subjected to previous collapse therapy. When fibrosis has supervened in a lung which has been extensively diseased there is likely to be gross crowding, displacement and irregularity of the bronchial tree. These gross changes can be demonstrated bronchographically, but in the conventional bronchogram it is frequently impossible to identify accurately the various bronchial divisions or even to determine their exact point of origin on the stem bronchus. Tomobronchography has provided the answer in such situations and an example of the assistance which it can afford is illustrated in Figs. 2A and 2B. A previous artificial pneumothorax or a thoracoplasty may produce a similar degree of anatomical disorganisation and, again, tomobronchograms may be required before the distorted bronchial tree can be clearly mapped out.

(3) *The demonstration of the relationship of a cavity or a solid focus to its associated bronchus.* Cavities or solid foci may not show up clearly on a conventional bronchogram and consequently it may not be possible to locate accurately their related segmental bronchi. In the case of a solid focus the study of the related bronchus and of the nature of its termination at or in the lesion can be of diagnostic importance, while with cavitated disease the outline of the draining bronchus may provide pathological evidence as well as anatomical information essential to the planning of surgery (Figs. 3A and 3B). In the course of this work it has been possible on a number of occasions to outline tuberculous cavities with the opaque medium (Keers *et al.*, 1956), producing a bronchographic pattern requiring differentiation from gross bronchiectasis. Tomobronchography has proved invaluable in differentiation as well as in permitting detailed study of the draining bronchus through which the medium had entered the cavity lumen.

(4) *The dissociation of any inadvertent bronchial filling on the contralateral side from the side under review.* Such inadvertent filling is by no means uncommon and can be a source of some confusion in interpretation. The potential value of lateral tomobronchography in clarifying such a situation needs no elaboration.

Conclusion

Tomobronchography is both expensive and time-consuming and its routine employment in association with every bronchographic examination is neither feasible nor necessary. There are, however, circumstances in which it can yield information of clinical importance which is not otherwise obtainable and we believe that a good case can be made out for its more frequent use in a restricted field.

On the basis of our experience in this unselected series we consider that its main value in pulmonary tuberculosis lies in the pre-operative investigation of certain cases in which resection surgery is contemplated, and we would suggest the following indications for tomobronchography:

(1) Cases with peripherally situat lesions, either solid or cavitated, especially where the disease i rently localised to a single segment.
(2) Cases in which the origin s known to have been much more extensive than the current aph would suggest.

(3) Cases which have had previous collapse therapy, either pneumothorax or thoracoplasty.

The choice between lateral or antero-posterior views in the individual case is a more difficult matter on which to offer guidance, but, broadly speaking, lateral views are more likely to be helpful in cases where the lower lobes or the right middle lobe are involved, while antero-posterior views are usually of more assistance in upper lobe disease.

The possibilities and the limitations of tomobronchography have yet to be defined, but it seems probable that it can provide something more than mere accurate anatomical localisation of lesions and that eventually deductions regarding bronchial pathology will be justified. As examples of the latter possibility, we would suggest that (*a*) the " rat tail " appearance noted in some subdivisions represents *complete* occlusion, (*b*) the narrowed, but blunt, termination of a bronchus is indicative of stenosis which is not yet complete, and (*c*) the rectangular termination is usually due to mucus in the bronchial lumen, except when it occurs exactly at the broncho-cavitary junction, when it can equally well be caused by the granulation tissue associated with active endobronchial tuberculosis. These ideas, however, are still hypotheses only and further study is required before they can be put forward as firm and proven facts.

Summary

(1) Experiences with bronchographic tomography in pulmonary tuberculosis, based on a series of 218 sets of tomobronchograms, are described.

(2) This method of investigation yielded information of clinical importance in 15 per cent. of the cases examined.

(3) As considerations of time and cost make tomobronchography unsuitable for routine use, an attempt has been made to indicate the type of case in which it may be most profitably employed.

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STEROID-TREATED TUBERCULOUS PLEURAL EFFUSIONS

By John Aspin and Helena O'Hara

From The Royal Hospital, Wolverhampton, and Prestwood Sanatorium, Stourbridge

The purposes of treatment in cases of acute tuberculous pleural effusion are twofold; firstly, by antibacterial drug treatment to reduce the risk of later development of other tuberculous manifestations (Emerson, 1957), and secondly, to bring about early and complete absorption of the fluid without loss of lung function consequent upon chest deformity.

In recent years, attempts have been made to hasten the absorption of fluid by repeated aspiration, instillation of antibacterial drugs, and appropriate physiotherapy. These methods, which are taxing to patient and clinician alike, have not always met with the success claimed by Mackay-Dick and Rothnie (1954).

These mechanical attempts to remove the by-products of the hypersensitive state leading to the effusion seem less attractive than attempts to control the hypersensitive state itself through the use of corticosteroids combined with antibacterial drug treatment.

Stimulated by reading Acheson's (1955) account of the experience of Sors and Trocmé (1954), who claimed that corticosteroid treatment brought about swift absorption of pleural fluid, we decided to investigate the value of this form of treatment.

The trial was confined to cases of acute recently developed pleural effusion in which a tuberculous ætiology seemed to be beyond reasonable doubt. The presence of peptic ulceration was excluded and weight, urine-tests for sugar and albumen, and chest radiography were checked weekly. Fluid intake was restricted and potassium chloride was given (1 g. twice daily).

By giving streptomycin (1 g.) and isoniazid (300 mg.) daily it was hoped to avoid any flare-up of underlying tuberculous lung lesions, and antibacterial treatment was continued for at least six months after the eventual withdrawal of the steroid drugs.

Eight cases were treated with corticotrophin, two with cortisone, and six of the later ones with prednisone.

Details of Treatment

Treatment of the first case was initiated in September 1955. A week later, when the fluid had cleared down to the costophrenic angle, the initial daily dosage of 20 units of long-acting ACTH given by injection was reduced to 10 units.

(*Received for publication October* 21, 1957.)

As we now believe, this reduction was a mistake. The hypersensitive or exudative state had been temporarily controlled but was not overcome. At the lower dosage, the next radiograph taken six days later showed a slight increase of fluid.

It looked as though by analogy with the ordinary course of untreated effusions and the behaviour of steroid-treated hypersensitive reactors to streptomycin and PAS a rather larger initial dosage ought to be continued for about two months, to give time for the subsidence of the hypersensitive state. Italian workers refer to the recurrence of exudation after too early withdrawal of steroids, and Sors and Trocmé comment upon one similar case.

At a dosage of 40-units daily of ACTH or (later) 20 mg. daily of prednisone given by mouth, we found that we could expect even massive mediastinum-displacing effusions to clear dramatically without aspiration down to the line of the seventh rib anteriorly or even further into the costophrenic angle in a fortnight, three weeks, or at most a month.

Further clearing of the costophrenic region seems to have been rather more sluggish with prednisone than with corticotrophin, and indeed it is now considered that any long period of replacement therapy with prednisone should be followed by a short period of ACTH treatment to boost temporarily depressed natural corticosteroid secretion.

The only extension of a lung lesion observed in this small series may have developed during a temporary hypocorticoid state following withdrawal of prednisone, and might have been avoided by final ACTH treatment. This patient's prednisone was withdrawn after twelve weeks and the left-sided spread was seen nearly six weeks later. The " rebound " cleared in another month under routine antibacterial treatment.

Analysis of Results and Discussion

Of 30 cases, 16 were given steroids. Thirteen of the 14 otherwise treated were diagnosed just before we began to use steroids, or did not initially come under our clinical control. One case gave a history of peptic ulceration.

Some cases in both groups had small tuberculous lung lesions, but in none could the effusion be considered secondary to chronic pulmonary tuberculosis.

In the 16 steroid-treated cases, fluid cleared down to the line of the seventh rib anteriorly (or further into the costophrenic angle) in an average of twenty-eight days. Only one minor loculation was left, and in the two cases in which there was slight falling-in of the ribs, this condition was present when treatment was started.

Among the 14 who had no steroids, 3 were treated by repeated aspiration, streptomycin, etc. The others were more conservatively treated. In the group of 14, it took an average of over sixty days for fluid to resolve to the line of the seventh rib anteriorly, even by counting as of only three months' duration the 3 cases in which resolution was materially longer delayed. In 6 cases there were loculations, three of considerable extent. In 2 there was marked residual deformity. One case had to have decortication.

Emerson (1957) found no evidence that antibacterial therapy reduced the duration of the effusions in his 102 cases. There was clearing with no more than residual obliteration of the costophrenic angles in less than three months in 42 of these patients, in three to twelve months in 44, and in one to three years in 9. The remaining 5 showed persisting moderate thickening after three years.

Pines (1957) found that residual pleural thickening was as common among those cases of tuberculous pleural effusion treated with chemotherapy as among those without. He did not, however, think that this residual thickening was of any immediate clinical importance.

Clearly the results are more favourable for the steroid-treated cases, and this form of treatment amounts in our opinion to a real advance in management. Although observation has extended to more than a year in only 11 out of 16 cases, we see no reason to fear extension of lung disease if antibacterial drug treatment is given, or other complications of steroid treatment if given with due precautions after suitable initial investigations.

Summary

A comparison is made of the progress with regard to resolution of fluid of 16 steroid-treated and 14 otherwise-treated acute tuberculous effusions of recent onset.

In the cases treated with ACTH (40 units daily) or prednisone (20 mg. daily) supported by streptomycin and isoniazid, the fluid absorbed dramatically without the need for other than diagnostic aspiration.

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LONG-TERM CHEMOTHERAPY IN PULMONARY TUBERCULOSIS

By Philip M. Ward

From Wooley Sanatorium, Hexham, Northumberland

The use of chemotherapy has so revolutionised the management of pulmonary tuberculosis that its historical relationship to the natural history of the condition is being forgotten. The combination of bed rest and fresh air has for long been the backbone of management of the disease, and it is against this background that the contribution of chemotherapy must be understood. Griep (1955), in assessing active treatment in the Netherlands during the previous twenty years, pays tribute to the efficacy of bed rest as the basis of all therapy, and admits that, in spite of increased efficiency of drugs and surgery, the nursing time has not decreased.

The full power of chemotherapy depends upon a combination of drugs retarding the emergence of bacillary resistance, and it is on work done in recent years on the optimum duration of drug-régimes that this paper seeks to offer some contribution.

Capel and Mitchell (1955), Tucker (1955), Tucker and Livings (1955), and Frazer (1956) are among those who testify to the value of long-term chemotherapy, and admit the value of bed rest whether drugs are given in hospital or at home. More recently Tobias (1956) has described a régime of ambulant chemotherapy, as used in South Africa when patients are unwilling to go to bed, and although there is no doubt that cases of relatively early disease without much systemic disturbance can be handled satisfactorily in this way it is felt, in company with the majority of present-day workers, that institutional treatment is beneficial to the more advanced cases still commonly seen today.

Present Investigation

With this in mind the efficacy of prolonged chemotherapy and bed rest was investigated at Wooley Sanatorium. An analysis was made of all patients discharged in 1955 and 1956, who had had at least six months' continuous bed rest and chemotherapy. These were all severe or moderately severe cases, and in selecting them those who had had recent operations, and all pregnancies, were discarded so that the 126 patients chosen, 45 females and 81 males, formed a uniform group of all those who had been treated by this method. Judged on admission lesions these fell naturally into three groups; firstly acute and subacute disease with perhaps thin-walled cavitation, including pneumonic and miliary lesions, secondly fibro-cavernous disease, essentially chronic, and thirdly solid lesions, sometimes with central cavitation.

The drug-régimes varied fortuitously. Some patients received daily Streptomycin 1 g., PAS 12-15 g. and INH 200-400 mg.; others were given equivalent daily doses of Streptomycin/PAS or Streptomycin/INH; while

(*Received for publication September* 16, 1957.)

others again had INH daily with Streptomycin and PAS every other day alternating with each other. These divergent régimes produced much the same results, as might be expected from the work of Tucker (1955), Reisner *et al.* (1955) and the Medical Research Council. In cases of bacillary resistance to one drug the other two were given daily; with multiple resistance all three were given daily, and only in a few cases were viomycin, terramycin or thiosemicarbazone used.

No difficulty was experienced in persuading patients to undergo this long régime, and none discharged themselves prematurely. Several in fact remarked gratuitously that the countryside was a pleasant change from the town, while others admitted that they could never have settled to treatment among the distractions of home surroundings. These points are worth noting when assessing institutional as against domiciliary treatment.

Results

Surgery, in the form of thoracoplasty or resection, was performed on some patients after the period of bed rest was completed, and the discharge-result is assessed with this in mind. A good result means good general condition relative to age and original lesion, sputum negative and disease under control. Table 1 confirms that the subacute group did well, many without surgery, and and it is noteworthy that there were 10 cases in which the surgeon advised deferment of operation, and in which clearing continued so that surgery was

Table 1.—Results according to Lesion Groups

Group	*Sex*	*Result*	*Totals*	*Surgery*
Subacute	Female	Good	28	12 (43%)
		Poor	7	
	Male	Good	39	7 (18%)
		Poor	2	
Chronic	Female	Good	7	5 (71%)
		Poor	1	
	Male	Good	33	17 (50%)
		Poor	4	2 (50%)
Solid	Female	Good	2	2 (100%)
		Poor	0	
	Male	Good	3	2 (67%)
		Poor	0	

ultimately unnecessary (*cf.* Blaha, 1956). The most satisfying results are perhaps seen in the chronic group, nearly half of whom did well without surgery, and in nearly all the rest sufficient improvement took place with chemotherapy to render surgery a therapeutic possibility.

Table 2 analyses the pre-operative results in those who had supplementary surgery. The subacute group shows better healing than the chronic group, and surgery in the former was more often a safety measure, while in the latter it was more often necessary in order to control the lesion. A combination of

TABLE 2.—PRE-OPERATIVE RESULT OF SURGICAL CASES

Group	*Sex*	*Pre-op. result*	*Totals*
Subacute	Female	Good	8
		Poor	4
	Male	Good	3
		Poor	4
Chronic	Female	Good	0
		Poor	5
	Male	Good	6
		Poor	13
Solid	Female	Good	0
		Poor	2
	Male	Good	0
		Poor	2

Tables 1 and 2 emphasises the relationship between medical and surgical treatment.

Radiological evidence of healing consisted of absorption of the lesions, and not replacement-fibrosis as was commonly seen in pre-chemotherapeutic days. Clinical confirmation of this was seen in the better general condition and breathing capacity during convalescence, and agrees with the observations of Auerbach (1955). There was no evidence that prolonged bed rest and chemotherapy leads to progressive lung fibrosis.

TIMING OF SURGERY

There are many who affirm that surgery should take place after only about three months' chemotherapy; others, such as Brown *et al.* (1956), Logan (1955), and Auerbach *et al.* (1955), recommend a much longer period. In this hospital a further series of patients, mainly in 1956, received surgery with good results after three or four months' drug treatment, but the result of the present

TABLE 3.—RESULTS ACCORDING TO SENSITIVITY GROUPS

Group	*Sex*	*Result*	*Totals*	*Totals combining sexes*
Unknown ..	Female	Good	27	Good 86
		Poor	4	Poor 6
	Males	Good	59	
		Poor	2	
Known sensitive ..	Females	Good	6	Good 16
		Poor	1	Poor 1
	Males	Good	10	
		Poor	0	
Known resistant ..	Females	Good	4	Good 11
		Poor	3	Poor 6
	Males	Good	7	
		Poor	3	

investigation confirms the value of the long-term régime, especially in cases with chronic disease.

Early surgery is, however, an advantage in the solid lesion, which responds poorly to chemotherapy but does well with surgery (Tables 1 and 2), and in cases showing bacillary resistance. Table 4 (column 7) suggests that better results are obtained in these resistant cases where surgery is employed.

Bacillary Resistance

All cases in this series had sputum tests towards the end of treatment, with sensitivity tests on those found positive, but though all had sputum tests

Table 4.—Analysis of Known Resistant Group

	Previous treatment	*Lesions*	*Sputum*	*Surgery*	*Bacillary resistance*	*Discharge result*	*Present condition*
Females	Yes	Chronic Bilateral	+ +	Nil	*S* p *I* H	Poor	Disease active Sputum positive
	No	Subacute Bilateral	+ −	Nil	s *P* I	Poor	Well but X-ray unstable
	Yes	Subacute Bilateral	+ −	Nil	*S* p I	Good	Well but X-ray unstable
	No	Subacute Bilateral	+ −	Nil	s P i	Good	Quiescent
	No	Subacute Bilateral	+ −	Resection	S P i	Good	Quiescent
	No	Subacute Bilateral	+ −	Nil	s P i	Good	Well but X-ray unstable
	Yes	Chronic Bilateral	+ +	Plasty	*S P I*	Poor	Disease active Sputum positive
Males	Yes	Chronic Unilateral	+ −	Plasty	*S* P *I*	Poor	Relapse and cor pulmonale
	Yes	Chronic Unilateral	+ −	Plasty	S p i	Good	Quiescent
	No	Subacute Bilateral	+ −	Nil	s *P* I	Good	Well but X-ray unstable
	No	Chronic Bilateral	+ −	Nil	S p i	Good	Quiescent
	No	Chronic Bilateral	+ −	Nil	*S* p i	Good	Non-quiescent Sputum negative
	Yes	Chronic Bilateral	+ +	Nil	s p *I*	Poor	Died
	No	Chronic Bilateral	+ −	Nil	S p I	Good	Quiescent
	No	Chronic Bilateral	+ −	Resection	S *P* I	Good	Quiescent
	Yes	Chronic Bilateral	+ −	Resection	S *P I H T V*	Poor	Died
	No	Chronic Bilateral	+ −	Plasty	S P I	Good	Quiescent

Sputum result on admission and discharge.
Sensitivity: small letters=sensitive; capital letters=partially resistant; capital letters in italic=completely resistant.
S=Streptomycin; P=PAS; I=Isoniazid; H=Nupasal (*o*-hydroxybenzal isonicotinyl hydrazone); T=Terramycin; V=Viomycin.

on admission not all positives were tested for sensitivity at that time. Of the 126 patients, 109 began sputum-positive and attained conversion, 14 were negative throughout and only 3 remained consistently positive. No cases of primary resistance were discovered. Table 3 shows results in relation to bacillary sensitivity, and since the results in the known-sensitive and unknown groups are similar it is a fair inference that those in the unknown group were, in fact, mostly sensitive.

Table 4 analyses the known-resistant group which comprises all those who developed some degree of resistance. Most of them were chronic and had bilateral disease, nearly half had had previous chemotherapy, and the sexes were evenly distributed. It is noteworthy that most of them attained sputum conversion, and also that the 3 persistently positive cases showed resistance.

A good result can often be obtained (*cf.* Beck, 1955) in these cases by increasing the dosage or changing the combination, and it is justifiable to continue drug treatment if the sputum can be rendered negative. To continue in the face of persistently positive sputum brings the danger of fostering infection of others by resistant organisms, a danger stressed by Murdoch and Grant (1955), Tarnowski (1955), and Beck (1955). The recent Medical Research Council survey (Fox *et al.*, 1957) shows the presence of more primary resistant cases than previous literature would suggest, and these workers find evidence of contact with drug-resistant organisms in these cases, but not in drug-sensitive controls. On the other hand, the prognosis of the positive resistant case is relatively poor; of the three in the present series, one is already dead and two are in very poor health.

Progress Report and Conclusion

The further progress of patients in this survey is encouraging, observation has ranged from two years to only three months, and this assessment is only

Table 5.—Analysis of all Cases (Total 24) Found Unfit on Follow-up

Group	*Sex*	*Discharge result*	*Present condition*
Subacute	Females	Good	U, U, *U*, *U*, RQ
		Poor	*U*
	Males	Good	U, U, A, A, A, *A*
		Poor	
Chronic	Females	Good	U, RQ
		Poor	*A*, *A*
	Males	Good	U, U, *U*, C
		Poor	R*UC*, *D*, *D*, D

Italicised cases are those showing bacillary resistance.
U=Well but radiologically unstable.
Q=Quiescent.
R=Relapse since discharge.
A=Active lesion, unfit for work, and needing further treatment. Sputum +
C=Cor pulmonale, with tuberculosis otherwise under control.
D=Dead.

an interim report. Of the 126 patients, 102 (80 per cent.) are deemed quiescent. The remaining 24 (20 per cent.) are reviewed in Table 5 and it is seen that nearly half of this group show bacillary resistance. The 11 cases labelled U are in good health clinically but show some radiological instability which may well settle down. As might be expected, the poorest results are seen in the chronic lesions, but it is gratifying to note how many of this type are still in good health.

These results are in line with the findings of Hoyle (1955), Steininger and Howard (1955), and Douglas and Horne (1956), and seem to confirm that rest and chemotherapy are well suited to the type of case for which they are intended.

Sincere thanks are offered to Dr. F. L. Wollaston, Medical Superintendent of Wooley Sanatorium, for his help and advice, and to all the Chest Physicians in the Newcastle Region for their assistance in following up the patients.

Summary

An enquiry into the efficacy of long-term bed rest and chemotherapy in a Sanatorium is described. The results are tabulated according to admission-lesion, and it is noted that good results were obtained even in fairly advanced cases.

The relationship to surgery of prolonged chemotherapy is assessed and its particular usefulness is seen again in the chronic cases. The relevant literature is also briefly reviewed.

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ACROMEGALY COMPLICATED BY DIABETES, PULMONARY TUBERCULOSIS, NEURITIC, CARDIAC AND JOINT LESIONS

By Philip Ellman and Leslie G. Andrews

From the Chest Unit, Plaistow Hospital, London

Acromegaly was first described in 1886 by Marie. Atkinson (1932) reviewed a total of 1,319 cases from the literature. Numerous complications of this condition have been described, including diminished sex function and impotence, thyrotoxicosis or myxœdema, stimulation of adrenal function, loss of vision and mental change. In 17 per cent. of acromegalic patients there is concurrent diabetes (Dovidoff and Cushing, 1927; Coggeshall and Root, 1940), and pulmonary tuberculosis often complicates diabetes (Boucot *et al.*, 1952). It is, however, rare to find all three conditions in the same patient, and we have found only three recorded cases in the literature (Savance, 1898; Ferrand, 1901; Tavares, 1954).

The case described here is that of an acromegalic man who developed severe diabetes and pulmonary tuberculosis. He also had a peripheral neuropathy, cardiomegaly and joint changes.

Case History

The patient, a man of 59, had pleurisy in 1938. His father had died of pulmonary tuberculosis.

In 1946, when 48 years of age, he began to notice enlargement of the hands and thickening of related skin. Simultaneously he had to take shoes a half size larger. The complete acromegalic picture gradually developed to give the classical facies with prognathism, thickened lips and nasal enlargement (Fig. 1). He developed a large tongue and a deep voice; the fingers were clubbed. His intelligence and memory remained normal although he appeared sluggish in movement and had a dysarthia. X-rays of his hands and feet showed bony enlargement with splaying of the phalanges, and a skull X-ray showed an enormous frontal sinus and deepened sella turcica. His spine and hips showed atrophic changes, the latter joints having bony outgrowths and remodelling. A mass miniature X-ray film taken in 1949 showed quiescent pulmonary tuberculosis.

In 1954 diabetes mellitus was discovered, which was well controlled initially on diet alone.

In June 1956 the patient was admitted to the Chest Unit at Plaistow Hospital under the care of one of us (P.E.). He complained of breathlessness, chest pain and hæmoptysis. On examination of the respiratory system the breath sounds were broncho-vesicular and there were scattered râles throughout both lung fields. In the cardiovascular system the apex beat was in the fifth left intercostal space, 4½ inches from the mid-line, and the blood pressure was 160/100, this being the highest recorded figure. No abnormalities were detected in the alimentary or central nervous systems. X-ray examination of the chest revealed infiltration in all zones of both lungs and cavitation at the right apex.

(*Received for publication July* 6, 1957.)

PLATE XIII

1930

1951

1956

SHOWING THE GRADUAL DEVELOPMENT OF THE COMPLETE ACROMEGALIC PICTURE.

To face p. 90

The sputum was positive for *Mycobacterium tuberculosis*, and streptomycin sulphate g. 1 intramuscularly daily, isonicotinic acid hydrazide (INAH) 100 mg. twice daily, and para-amino salicylic acid (PAS) therapy 20 g. daily, was commenced. The PAS was stopped after one month as this was causing bouts of diarrhœa.

It became necessary to start treatment first with a mixed dose of soluble and protamine zinc insulin and later to amend this to soluble insulin eight-hourly, as the diabetes increased in severity. During this period he developed a tuberculous ischio-rectal abscess which required incision and drainage; he also had multiple boils on the neck.

In February 1957, when the tuberculosis and diabetes were under better control, the patient complained of difficulty in moving his feet. He was found to have impaired sensation of both feet to pin-prick, and to light touch on the left. Deep muscle pain was absent on the left; dorsal and plantar flexion of the right foot were present but weak. On the left side there was complete foot-drop and no voluntary movement could be obtained. These changes were due to a rapidly advancing peripheral neuritis. The feet were splinted and pyridoxin and cyanocobalamin therapy was initiated as the neurological changes could have been due to the INAH treatment.

In April 1957 the patient became pyrexial again and his E.S.R. rose to 110 mm. per hour. The urine was free from Bence-Jones protein and a sternal marrow puncture was normal. The plasma electrophoretic pattern showed a reduction of albumin and an increase in the globulin fraction. He developed congestive cardiac failure which responded partially to digitalis and he gradually deteriorated until death occurred on May 15, 1957.

At the time of death, despite the pyrexia and elevated sedimentation rate, no abnormal pulmonary physical signs could be elicited, and a tomogram of the right apex of the chest showed almost complete cavity closure.

Necropsy Findings (Dr. Woodhouse Price)

The enlarged feet, hands, jaw and skull bones were consistent with acromegaly. The pituitary fossa was enlarged.

The pituitary was enlarged. The normal tissue, containing mucoid (basophil) and acidophilic cells and a few chromophobe cells, was confined to a rim of tissue surrounding a large acidophil adenoma. This was composed of poorly granulated cells with larger, more typical acidophils in some areas.

The lungs showed emphysema, œdema, old healed and calcified tubercles in both apices, and a solitary caseating mass 1 cm. in diameter at the right apex. Microscopy of this mass confirmed a caseating tuberculosis.

All the heart chambers were grossly enlarged. The coronary arteries were calcified; the pericardium was densely adherent.

In the liver there was nutmeg congestion, with lymphocytic infiltration of the portal areas, reduplication of the bile ducts, and commencing fibrosis.

In the pancreas there were several abnormal vessels, one showing gross intimal hyperplasia, and others showing less obvious intimal change, but with infiltration of the adventitia with inflammatory cells. (Similar vascular changes were seen in the spleen and epididymis.)

One kidney had a small infarct in it. The testes showed fibrosis and hyalinisation of most tubules and marked Leydig cell atrophy.

The adrenal and thyroid glands, the brain, spinal cord and lumbo-sacral nerves were all normal.

Discussion

Diabetes occurring concurrently with acromegaly has been described by Hansemann (1897), Shepardson (1944) and Natelson (1955). Dovidoff and Cushing (1927), in a review of 100 cases of acromegaly, found glycosuria in 25 per cent. and diabetes in 12 per cent. Coggeshall and Root (1940), in a follow-up of these 100 cases together with a further 53 cases, found glycosuria in 36 per cent. and diabetes in 17 per cent. Joslin *et al.* (1952) were only able to find 9 cases of acromegaly and 3 of gigantism in 30,000 patients attending a diabetic clinic. This is not surprising as acromegaly is not a common disease and only one-sixth of the cases have diabetes. In Coggeshall and Root's (1940) cases the average time interval between the onset of the acromegaly and the diabetes was 9·5 years. In our case the interval was 8 years. Their cases developed pyogenic infections, arteriosclerosis with gangrene, coronary atherosclerosis and diabetic coma. None were recorded as having peripheral neuritis or pulmonary tuberculosis.

Acromegalic diabetes may be of all degrees of severity and even insulin resistant. It does not differ essentially from ordinary diabetes, but the mechanism of hyperglycæmia is probably twofold: the release firstly of pituitary diabetogenic hormone and, secondly, of adrenocorticotrophin (McCormick *et al.*, 1951).

The frequent association of diabetes and pulmonary tuberculosis is well known. Weiner and Kavee (1936) in a comparison of diabetic and non-diabetic patients with pulmonary tuberculosis found pleural thickening twice as common in the non-diabetics. This, they thought, accounted for the more rapid development of tuberculosis in the diabetic subject. Tuberculosis outside the lungs is rare in diabetics except in combination with pulmonary tuberculosis.

Acromegaly together with diabetes and tuberculosis is a much rarer combination. In Atkinson's (1932) review of 1,319 cases of acromegaly, 265 were examined post-mortem. Of these there were 8 cases with tuberculosis, 5 of which were pulmonary. Of the total cases only 2 had diabetes as well as tuberculosis (Squance, 1898; Ferrand, 1901). Tavares (1954) has described a case in which the diabetes was resistant to insulin. In our case not only was the diabetes difficult to stabilise, but a resistance to all the major anti-tuberculous drugs developed. Despite this the lung lesions improved. The ischio-rectal abscess was also of tuberculous ætiology. Inability to check the tuberculosis with drug therapy probably accounted for the difficulty in controlling the diabetes. There is a tendency for any existing tuberculous focus to break down in acromegaly independent of diabetes, probably because of the circulating excess of adrenal cortical hormones.

Peripheral neuritis complicates 50 per cent. of cases of diabetes mellitus. Hirson *et al.* (1953) found symmetrical polyneuritis rare. Rudy and Epstein (1945) described pain and sensory disturbance as the main change. Rundles (1945) in an exhaustive survey of the subject, makes no mention of the purely motor form of the disease, but Garland and Taverner (1954) have described diabetic myelopathy without any objective sensory disturbance. The neurological changes may be entirely due to pathological changes in the peripheral

vessels (Woltman and Wilder, 1929), but Martin (1953) found no evidence of a vascular disorder and Hutchinson and Liversedge (1956) concluded that vascular ischæmia played only a minor role in the ætiology of peripheral neuritis. In our case the nervous manifestations were atypical of diabetes, the motor symptoms predominating.

Pronounced cardiomegaly is known to occur occasionally in acromegaly and may be due to a rise in blood pressure (Seyle, 1949), although considerable cardiomegaly can occur in the absence of hypertension (Evans, 1956). Despite a cor bovinum, the blood pressure was never greatly elevated, atherosclerosis was not very prominent, the fundi remained normal and no nephropathy developed.

Joint changes in acromegaly have been described by Kellgren *et al.* (1952). The bony atrophy, outgrowths and remodelling occurring in the hips of our patient are consistent with the acromegalic joint lesion.

Summary

Diabetes mellitus occurs in a high percentage of patients with acromegaly. A most unusual case is described with the very rare combination of pulmonary tuberculosis, diabetes mellitus, diabetic neuropathy, pyogenic infections, cardiomegaly and arthritis, all complicating long-standing acromegaly.

The slides of the pituitary were kindly reported on by Dr. A. G. E. Pearse, and we are very much indebted to Dr. J. Lee for his help on the diabetic side and for many valuable suggestions.

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LAURENCE STERNE: A WITTY CONSUMPTIVE

By Sir Arthur MacNalty, K.C.B.

Tristram Shandy and *A Sentimental Journey* are admittedly English classics. Sir Walter Scott said of Sterne: "In the power of approaching and touching the finer feelings of the heart, he has never been excelled, if indeed he has ever been equalled," and added he was "one of the most original geniuses whom England has produced." Carlyle classed him with Cervantes among the great humorists of the world. Even Thackeray, who liked neither the man nor his writings, felt obliged to include Sterne in his lectures on *The English Humourists*. He was a notorious plagiarist, notably from Burton's *Anatomy of Melancholy*; his Rabelaisian humour shocked his contemporaries and later the Victorians. But Uncle Toby and Corporal Trim—and we may add Yorick himself—"more than entitle the author to a free pardon for his literary peculations, his indecorum and his affectations." For the greater part of his life he waged a heroic struggle with the tubercle bacillus. The jester made the world laugh, but a death's head grinned behind his mask.

Laurence, the son of Roger Sterne and Agnes Hebert, was born at Clonmel in the south of Ireland on November 24, 1713. His father served as an ensign in Marlborough's wars, and died after contracting a fever in Jamaica when his son was seventeen. Laurence had a chequered and ill-nourished childhood, following the regiment and accompanying his parents in a number of campaigns. When he was eleven years old, his wealthy uncle, Richard Sterne, and later Richard's son, took charge of the boy's education. He went to school at Halifax and afterwards entered Jesus College, Cambridge, as a sizar in 1733. In his last year at the University he awoke one night to find that he had bled "the bed full" from a hæmorrhage of the lungs. Pulmonary tuberculosis had declared itself and was to dog his footsteps for the rest of his life. He met every onslaught of the disease with courage and a jest, leading Death "a dance he little thinks of," and with admirable fortitude repelled his adversary. In January 1736 Sterne took his B.A. degree and four years later proceeded to M.A. In 1736, too, he was admitted to deacon's orders and appointed curate to the vicar of St. Ives. In 1738 he became priest and received the living of Sutton-in-the-Forest, a village near York, through the patronage of his uncle, Dr. Jaques Sterne, Canon of York and Archdeacon of Cleveland. In 1740 he secured a prebend in York Cathedral and another minor prebend.

Sterne had already fallen in love with Elizabeth Lumley, a cousin of Elizabeth Montagu, the famous Bluestocking. Miss Lumley "fell into a consumption," and on her supposed deathbed left Sterne all her fortune. This touched the young clergyman's sentimental heart. "This generosity

(*Received for publication August* 9, 1957.)

overpowered me. It pleased God that she recovered and I married her in the year 1741," he wrote. The union of two consumptives is seldom wise and Sterne eventually tired of his wife. But he looked after her as a husband and he adored their daughter, Lydia. The latter seems to have contracted her parents' malady—she could hardly escape contact infection—for she suffered from " asthma," a term often descriptive of pulmonary tuberculosis in the eighteenth century. Smollett, the novelist, who died of tuberculosis, regarded his disease as an " asthmatical disorder," and was offended when the physician at Montpellier ascribed his symptoms to " des tubercules du poumon."

A country life with open-air exercise was beneficial to Sterne. He wrote sermons, political squibs for his uncle and attended diligently to his two parishes of Sutton and Stillington, during which time " books, painting, fiddling and shooting " were his chief amusements. At Skelton Castle he enjoyed the hospitality and society of his college friend, John Hall Stevenson, the author of *Crazy Tales*. Sterne was also a philanderer of the Platonic and ultra-sentimental order. " I must ever have some Dulcinea in my head; it harmonizes the soul," he wrote. This weakness was the more unsuitable in a parson and has led to aspersions on his moral character which appear to have been unfounded.

Sterne's genius flowered late. It was not until his forty-sixth year that he began to write the first two volumes of *Tristram Shandy*, " the great humour of which consists in the whole narrative going backwards " (Horace Walpole). It was published in London in January 1760 and brought the author fame. In March Sterne went to London, where he was exposed to late hours and excessive hospitality. This undermined his health. His wife had been ill for some months; her tuberculosis was accompanied by a mental breakdown with delusions. There were some compensations. Sterne's portrait was painted by Reynolds, and he was given the additional living of Coxwold, 15 miles from York, which was high up amid green hills. Here he wrote the third and fourth volumes of *Tristram Shandy*. In December he paid another visit to London which lasted nearly six months. He was lionised more than before, " fourteen dinners deep engaged." In June 1761 he returned to Coxwold, but was back in London by the end of November with his fifth and sixth volumes of *Tristram*, to be taken up by Lord and Lady Spencer. Again fatigue and late hours exacerbated his disease and he suffered the worst hæmoptysis he ever had. He was nursed by his friend Mrs. Vesey, " a charming nurse." The physicians warned Sterne that another winter in England would be his last, and considered his state hopeless of recovery.

England was at that time at war with France, but Sterne obtained a safe-conduct, borrowed £20 from Garrick, and went to France. He was very ill during the crossing. In the meantime, his wife had recovered but Lydia's " asthma " was worse. He sent for them to join him in Paris, but before they arrived he had another severe hæmoptysis for which a surgeon bled him in both arms. The reunited family travelled to Toulouse, where, during an epidemic, Sterne hovered on the brink of death for six weeks. In June 1763 he went to Bagnères in the Pyrenees for spa treatment, but the sharp mountain air was

bad for his lungs. The winter was spent at Montpellier, where his wife and daughter chose to remain. In March 1764 Sterne arrived in Paris and preached before the British ambassador. In May he had another serious hæmoptysis. After spending June in London, he returned to Coxwold.

In January 1765 he published the seventh and eighth volumes of *Tristram Shandy*. He was then in London, where the old round of dinners and activities caused recrudescence of his malady. He moved to Bath surrounded by a train of admirers. In April he was in London again. In May he was ill and had hæmoptysis. His health improved once more with rest at Coxwold.

In October he went to London and set out on his travels, partly recorded in *A Sentimental Journey through France and Italy*. After social gaieties he was ill in Paris. By November he was in Italy and spent Christmas at Rome. In mid-January the traveller reached Naples, where his health improved. With characteristic optimism, he described himself as "fat, sleek and well-liking." On his return journey through France he visited his wife and daughter at Franche Compté. By the end of June he was back at Coxwold working on the last volume of *Tristram Shandy*.

Sterne's health now became gravely impaired; he had a persistent cough and hæmoptyses recurred with alarming frequency. In January 1767 he struggled to London and engaged in a sentimental interlude with Mrs. Draper, to whom he addressed the *Journal to Eliza*. He had a severe hæmoptysis in March, and Eliza's departure for India to rejoin her husband left him "worn out by fevers of all kinds." In April he was further weakened by a surgeon who took 12 ounces of blood from him. Like Goldsmith, he took James's powder with bad results. The doctors attributed his symptoms to venereal disease though Sterne assured them he had run no risk of infection. They gave him a course of mercury which made him worse. Back at Coxwold in May, "a bale of cadaverous goods consigned to Pluto and Company," his health again improved. He drove out in his chaise, went to Harrogate to take the waters and settled Mrs. Sterne and Lydia, on their return from France, in a house in York. He was now writing *A Sentimental Journey* (published in the following February), and received many offers of preferment in the Church, which his failing health did not allow him to accept.

January 1, 1768, found Sterne settled in London in his old rooms at 41, Old Bond Street. He struggled to fulfil social engagements, but soon became too ill. By March he had taken to his bed with influenza and pleurisy, and on the 18th of that month he died, watched by Craufurd's footman. He was buried in the new burying-ground of St. George's Parish near Tyburn. It is said his body was dug up by "Resurrection men" and was recognised on the dissecting table in the Cambridge School of Anatomy.

Commentary

Sterne's form of pulmonary tuberculosis appears to have been of the fibro-caseous type with recurrent attacks of hæmoptysis. His case-history shows that he had considerable powers of recuperation, and with modern treatment his

life might have been further prolonged and his disease arrested. The treatment of those days—venesection, for example—did not benefit him, but the rest, good nutrition and pure air of Coxwold did. The London visits, late hours and excitement were disastrous. He endured suffering and domestic unhappiness with the courage of his genius.

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REVIEWS OF BOOKS

Sir Robert Philip. 1857-1939. *Memoirs of his Friends and Pupils.* London: N.A.P.T. 1957. Pp. 96. 12s. 6d.

Sir Robert Philip, the centenary of whose birth is celebrated in this short symposium of his life and work, was one of those dignified, cultivated gentlemen of the medical profession who seem, alas, to be a diminishing asset. It is well that the present generation of doctors should be given a reminder of the ethical standards for which he stood, and of the value of the methods which he employed in his professional activities generally, and especially in his teaching. It is not for nothing that Dr. Fergus Hewat, who writes the first article in this charming little book, refers to his old chief as one of the " great clinical teachers, who combined lucid explanations with a delightful delivery, a wide outlook on disease, and the regular attendance of each lecturer, regarded by our teachers in those days as a point of honour to their students."

Most biographies of great men, coming from the pen of a single writer, are apt to suffer to some extent from the personal preconceptions of the author, and the majority of medical authors can scarcely claim to be trained historians. For this reason it is as refreshing as it is salutary to peruse this volume, which gives the recorded impressions of a number of persons, including some non-medical writers, all closely associated with this distinguished pioneer. The net result is, in all probability, a more accurate and illuminating picture of Sir Robert as he really was. The volume has been produced in a way which makes it attractive to see and handle. The accounts given by the various contributors, all written from slightly different angles, combine historical accuracy with humour and with no little grace of literary style. The work as a whole is truly delightful, and the writer feels privileged to have been asked to review it for this Journal.

MAURICE DAVIDSON.

The Diagnosis and Treatment of Pulmonary Tuberculosis. by PAUL DUFAULT, M.D., Medical Director of the Rutland State Sanatorium, Massachusetts Department of Public Health. Second Edn. London: Henry Kimpton. 1957. Pp. 426, 162 illustrations. 67s. 6d. net.

The reader will find here a good account of pulmonary tuberculosis in a comparatively small space. Special emphasis is laid on diagnosis and treatment, and chapters are included on Pathology by Dr. Reynolds Crane and on Pulmonary Function by Dr. Oscar Feinsilver. Particular attention is given to the use of antibiotics and chemical substances in treatment, and to the various surgical procedures " perfected " during the last decade. The logic of their application and the results which may be expected are discussed.

The book is produced in an attractive form, it is clearly printed, and the illustrations, in the majority of cases, are excellent. Exception may be taken to the view expressed on p. 392 that " the practice of giving antibiotics in the absence of positive sputum is generally unsound and should be discouraged." This appears to differ from an earlier statement on p. 262 that " it is quite possible, however, that early lesions be discovered before the breakdown of any tubercles. Observation of a month or two should then suffice to determine whether or not the lesion is due to an active process and then chemotherapy should be instituted, especially when the patient is young."

Other views which may not meet with universal acceptance nowadays include the opinion that a prolonged period of bed rest, up to ten months or a year, may be required as a fair average when dealing with young individuals with minimal or moderately advanced lesions, as also the emphasis laid on the importance of admission to hospital or sanatorium for the first stages of treatment. The chapter on Differential Diagnosis is particularly valuable for those lacking a thorough knowledge of general medicine.

This is a good book, written in a clear and refreshing style, which can be confidentially recommended. G. E. BEAUMONT.

Advances in Tuberculosis Research. Vol. 8. *B.C.G.—A Discussion of its Use and Application.* Edited by H. KIRKHAUSER (Basel) and H. BLOCH (Pittsburgh). Oxford: Blackwell Scientific Publications. Pp. 316. 60s.

This volume contains a series of papers on all aspects of B.C.G. by eminent authorities of various nationalities. It brings into one book much information which is scattered in a large number of journals. The only other book with similar content likely to be well known to British readers is that by Irving. As the title suggests, this book goes more fully into the research aspect.

Birkhaug in the paper on " Methods of Vaccination " gives a very unbiassed account of the advantages and disadvantages of the various methods, and it is interesting to note that for routine work he seems to favour the multiple puncture method. Certainly its use requires a much lower standard of technical skill. The oral method is comprehensively dealt with by A. de Assis from Brazil. He does not claim 100 per cent. success, but thinks that in dealing with vast numbers in less advanced nations it has strong claims. He favours the single large dose method, and quotes several papers which claim that repeated doses may reduce the skin sensitivity, though this is denied by others.

Other papers which specially interested your reviewer were those of Horwitz and Johannes Meyer, giving a very full account of untoward reactions observed after vaccination, and by Maude on the lack of danger incurred by vaccination of subjects who have had or are undergoing tuberculosis infection.

J. A. Meyers concludes with a summary of the views opposing B.C.G., but many of the adverse explanations of the apparent success of B.C.G. seem far-fetched. The loss of the value of the tuberculin test will only measure up to the value of B.C.G. when tuberculosis is much nearer eradication.

Many of the authors rightly insist that many contradictory papers are due to variation in the B.C.G. in different countries, and the lack of knowledge of the number of viable bacilli in the material at the time of inoculation.

The multiple authorship illustrates very well the views held in different countries. All the papers are of a high standard, and at the end of each there is a full bibliography. The insertion of the authors' addresses is unusual but welcome. The book can be unreservedly recommended to all who are interested in the subject, except for the price (60s.). F. H. YOUNG.

The Anatomy of Congenital Pulmonary Stenosis. By SIR RUSSELL BROCK, M.S., F.R.C.S., F.A.C.S.(Hon.). London: Cassell and Co. Ltd. Pp. 114. 30s.

There are few modern publications which are likely to become classics, but this monograph by Sir Russell Brock, who was the first surgeon to carry out a direct operation for pulmonary stenosis, is a most important contribution

to medical literature. It may not be the last word on the subject, but it is certain to hold its place as a classic.

This book starts with a scholarly exposition of the embryology and comparative anatomy of the bulbus cordis in the development of the heart and its relationship to the right ventricle and the closure of the interventricular septum. Credit is given to the writings of Peacock (1866) and to Keith (1904 to 1924) in this section. Until recent years the subject has been of academic interest only, but it is remarkable how accurate were the observations of these previous investigators. The author has added greatly to their knowledge by his own observations based on his experience in dealing with the various anomalies.

Now that it is possible to correct so many congenital deformities of the heart by surgery, their anatomy is no longer a matter of pure academic interest. It is essential that cardiologists and cardiac surgeons should recognise the practical implications associated with the anatomical variations of the actual defects. To the uninitiated the term pulmonary stenosis suggests stenosis of the pulmonary valve. If the title of the monograph had been " the anatomy of congenital obstruction to the outflow from the right ventricle " it would have been too ponderous, but it would have given a better description of the theme of the work.

This small volume gives a lucid explanation of the various anomalies. The illustrations are excellent and are the result of practical operative experience. No clinician who undertakes responsibility for the management of patients with congenital heart disease can afford to neglect this valuable contribution. The information that it contains cannot be found elsewhere.

VERNON C. THOMPSON.

An Introduction to Chest Surgery. By GEOFFREY FLAVELL. London: Oxford University Press. 1957. Pp. 354. 180 Illus. 30s.

First of all, congratulations are due to the author and publishers on the production of such a sizable and profusely illustrated book at so low a price (30s.). Secondly, the author must be congratulated on succeeding in such large measure in achieving what he set out to do, namely to write a readable textbook sufficiently dogmatic to satisfy the student's needs.

The whole field of thoracic surgery is covered; there are sections on pulmonary tuberculosis, non-tuberculous pulmonary disease, the œsophagus and diaphragm, and on cardiac surgery. All the more usual thoracic operations are described in sufficient detail, but the more complex and troublesome ones have rightly been excluded.

The basic anatomical facts are given and pre- and post-operative care is adequately described. Throughout the book points are made by individual case histories and the results of surgery are illustrated by the author's own figures.

In a field where progress has been, and still is, so rapid much has been brought up to date, and although there are a number of statements which would not command universal approval, the author stresses that the book is based on personal experience. For the same reason references are excluded.

There is perhaps one major criticism which should be voiced: there is no section on respiratory physiology and the methods of assessment of pulmonary function. As these methods are in common and increased use the

student should be aware of the main principles upon which they are based. Perhaps this omission could be corrected in the second edition which will undoubtedly be required.

J. R. BELCHER.

Bronchopulmonary Diseases. Basic Aspects, Diagnosis and Treatment. Edited by EMIL A. NACLERIO, M.D., Chief of the Thoracic Surgical Services, Harlem, and Columbus Hospitals, New York. London: Cassell and Co. Ltd. Pp. 984. 719 Illus. £8 17s. 6d.

Many aspects of this work are excellent and comprehensive; others are inadequate and sketchy, which is somewhat surprising in such a work where the Editor states that the "basic motive in preparing this volume has been the need for an up-to-date, compact, authoritative and comprehensive compilation on the diagnosis and management of broncho-pulmonary diseases" referred to so frequently as "B.P.D." There are 142 separate contributors to this specialised field of medicine. One asks oneself, are all these contributors really necessary, and might not too many cooks spoil the broth? Is it, for example, really necessary under the general heading of "Roentgenology" to have separate chapters or subsections, each written by a different contributor, on "Problems in Roentgen differential diagnosis," "fluoroscopy," "radiographic technique," "bronchography," "angio-cardiography" and "reliability of chest radiography"? And if so, why has not tomography also been singled out for a special subsection? One feels that specialisation is being carried to extremes, apart from conducing inevitably to much overlapping and repetition. Having said this, one must equally admit that the book is admirably produced, is undoubtedly up to date, the 719 illustrations are of excellent quality, and the references are for the most part comprehensive.

The emphasis on certain aspects of embryology, developmental anomalies, anatomy, physiology and pathology are welcome, as indeed is the section on "Heart and Lung Diseases" with its subsections on "Chronic Pulmonary Disease of the Heart" and "Pulmonary Diseases secondary to Heart Diseases."

The section on "Pulmonary Manifestations of Systemic Diseases" serves to integrate the speciality with general medicine. The expert contributions on pulmonary tuberculosis, pulmonary suppuration, benign and malignant tumours, and "coin" lesions and solitary tumours, are of considerable interest.

Although the price, £8 17s. 6d., is perhaps prohibitive to people bereft of dollars, notwithstanding its shortcomings, the book contains a fund of useful information from experts on the other side of the Atlantic.

Brompton Hospital Reports, Vol. XXV, 1956. London: Lloyd-Luke (Medical Books) Ltd. Pp. 312. Illus. 15s.

These Reports, a collection of papers by members of the staffs of the Hospitals for Diseases of the Chest and the Institute of Diseases of the Chest, continue to maintain the high standard to which we are accustomed. Although all the papers have already appeared in the medical press, it is extremely valuable to clinicians in this wide field of medicine to have the contributions in a compact form. It is difficult to single out any particular article, for they are all of high standard. The increasing number of contributions on diseases of the heart are in keeping with modern trends and all the articles are

admirably illustrated. The editors and publishers are to be congratulated on a high-quality production at very modest cost. PHILIP ELLMAN.

B.C.G. Vaccination against Tuberculosis. By SOL ROY ROSENTHAL, M.D., Ph.D., Director Institution for Tuberculosis Research of the University of Illinois, and Medical Director of the Research Foundation, etc. London: J. and A. Churchill Ltd. 1957. Pp. 389. 55s.

From the Preface it would appear that this book, written primarily for the medical profession, has been designed to stimulate a more extensive use of B.C.G. vaccination in the United States and elsewhere. The more recent work in this field is discussed against a background of immunity to tuberculosis in general, the history of the development of B.C.G. and the response of the host. The preparation and standardisation of the vaccine and the routes and methods of administration are given in some detail, containing much of the author's own original work; this is followed by an account of the untoward reactions and virulence which may be encountered in man and the effect of vaccination with B.C.G. on those already infected with tuberculosis.

Three authors whose names are well known have contributed short chapters: Weill-Hallé, the first to use B.C.G. in the human subject; Wallgren, whose work in Sweden is so widely appreciated; and Camille Guérin, the last surviving member of the band of pioneers, who has written a fascinating and nostalgic account of the early work carried out at Lille.

The book has naturally been concerned with making out the best case possible for the use of B.C.G. inoculation, and few would deem this object unworthy; yet balance has been preserved throughout and the views which have been expressed antagonistic to the use of the vaccine, as well as chemoprophylaxis with isoniazid, have been given their place.

Illustrations have been well chosen and well reproduced. The bibliography at the conclusion of each chapter is full.

The author has been engaged in this sphere of work for over a quarter of a century and in this book he has summarised the essentials of his knowledge and experience. The serious student of tuberculosis will derive valuable information from it. N. LLOYD RUSBY.

BOOKS RECEIVED

The following books have been received and reviews of some of them will appear in subsequent issues.

Current Medical Research. Report for the year 1955/6. London: H.M.S.O., 1957. Pp. 56. 2s. 6d.

Annual Reports of the County Medical Officer and the Principal School Medical Officer, 1956. Published by the County Council of the West Riding of Yorkshire.

Recent Trends in Chronic Bronchitis. By Neville C. Oswald. London: Lloyd-Luke. 1958. Pp. vii+200. Illus. 30s.

Statistical Review for England and Wales for 1955. Part 3. London: H.M.S.O. 1957. Pp. 274. 11s.

Keeping an Eye on your Chest. Annual Report 1956-57. London: NAPT. Pp. 76.

Tuberculosis—Every Physician's Problem. By J. Arthur Myers. Oxford: Blackwell Scientific Publications. Pp. 200. Illus. 57s. 6d.

REPORTS

NAPT ANNUAL REPORT 1956-57

THE report deals with subjects including The First Tuberculosis Clinic, The Chest Physician To-day, The NAPT and Chest Diseases, Bronchitis, Smoking and Lung Cancer, Air Pollution and BCG and Vole Vaccination.

Concerning *tuberculosis*, it emphasises that there are more than 340,000 patients on the registers of chest clinics in England and Wales. It also notes that *chronic bronchitis* causes 30,000 deaths a year in England and Wales, and disables thousands more. A year or two ago it caused the loss of more than 25 million working days. The mortality in the United Kingdom is between twenty and fifty times as great as in Scandinavia.

Emphasis is also laid on *smoking and cancer of the lung*, urging that those who smoke heavily should cut down their smoking. The number of deaths from cancer of the lung has risen from about 2,000 in 1931 to 17,000 in 1955. More heavy smokers die from lung cancer than do non-smokers, and cigarette smoking is more dangerous than pipe smoking. The longer a person has smoked, the greater becomes his liability to fall a victim to the disease.

TUBERCULOSIS STATISTICS, ENGLAND AND WALES, 1938-55*

IN an analysis of trends and geographical distribution Dr. W. P. D. Logan and B. Benjamin give a full review of the facts. The study first sets out the general situation of tuberculosis morbidity and mortality in England and Wales, and shows the trends in recent years against the background of the pre-war situation. It then goes on to survey the notification rates of respiratory tuberculosis from 1938 to 1955 and examines the geographical distribution of notifications of respiratory tuberculosis in 1954-55 with regard to England and Wales as a whole and its larger administrative units. There is no doubt that during the last fifteen years mortality from tuberculosis has declined rapidly, but the reduction in notification rates has come much more slowly. Improved case-finding has resulted in earlier notification than formerly and, on the whole, cases currently notified represent less infectious forms of the disease than ten years or so ago. They point out that the proportion of newly notified cases of tuberculosis from which bacilli have been recovered had fallen from about 60 per cent. in 1938 to 41 per cent. in 1955. Summarising the situation as far as respiratory tuberculosis is concerned, the picture is of a tuberculous population (known and unknown) of the order of 375,000 persons of whom perhaps 45,000 are sputum positive and therefore infectious. While it seems likely that improvements in case-finding have reduced the period between onset and detection of disease (Lowe and Geddes, 1953), the total known tuberculous population is apparently still increasing, though there is evidence of a quickening reduction in the number of infectious cases.

In this picture they have left out of account other sources of spread of infection, notably milk-borne bovine tuberculosis which, though much reduced by improved dairy hygiene (including pasteurisation), still makes a contribution to the development of non-respiratory tuberculosis. Non-respiratory disease (not all of bovine origin) adds 36,000 cases.

The known infector pool is still large; the emptying of the unknown into the known infector pool could, state the authors, be more rapid.

* General Register Office. Studies on Medical and Population Subjects, No. 10. Published by H.M. Stationery Office. Pp. 56. 4s.

NOTES AND NOTICES

THE THORACIC SOCIETY

THE Spring Meeting of the Society will be held in the premises of the Zoological Society on March 7 and 8, 1958. The Summer Meeting will be held in Copenhagen on July 23, 24 and 25, 1958.

THE BRITISH TUBERCULOSIS ASSOCIATION

THE programme for 1958 includes a meeting on February 28 in conjunction with the Metropolitan Tuberculosis Societies; a Provincial Meeting at Cambridge on March 28 and 29 in co-operation with the East Anglian Thoracic Society; and the Annual Conference on July 1-4 in co-operation with the National Association for the Prevention of Tuberculosis.

The B.T.A. Prize. The Association is offering a prize of £50 for an original unpublished work on tuberculosis by a member of the Association during the year 1958. Details may be obtained from the Administrative Secretary.

NAPT COMMONWEALTH CHEST CONFERENCE

INCORPORATING THE ANNUAL CONFERENCE OF THE BRITISH TUBERCULOSIS ASSOCIATION

THE Commonwealth Chest Conference organised by the National Association for the Prevention of Tuberculosis and incorporating the Annual Conference of the British Tuberculosis Association, will be held at the Royal Festival Hall, London, from July 1 to 4.

The 1958 Conference will be wider in scope, as it will deal not only with tuberculosis but with other diseases of the chest and heart.

The provisional list of subjects for discussion includes the World Anti-Tuberculosis Campaign, Pulmonary Disease—a Malady of Environment, Cardiac Disease in its Social Aspects, Thoracic Surgery in Pulmonary Disease and the Problem of Lung Cancer.

AMERICAN COLLEGE OF CHEST PHYSICIANS

FIFTH INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST

THE Fifth International Congress on Diseases of the Chest, sponsored by the American College of Chest Physicians, will be held in Tokyo, Japan, September 7-11, 1958. The Congress will be presented under the Patronage of the Government of Japan and the Japan Science Council.

Scientific papers, panel discussions, fireside conferences and motion pictures will be presented on the following subjects:

Radiation Hazards.
Coronary Disease.
Occupational Diseases of the Chest.
Benign and Malignant Chest Tumours.
Tuberculosis.
Cardio-pulmonary Function Studies.
Asthma and Emphysema.
Cardiovascular Surgery.
Effect of Jet Air Travel in Chest Disease.
Broncho-œsophagology.
Tropical Diseases of the Chest.
Ætiology of Lung Cancer.
Paediatric Cardiology.
Metabolic Disorders.
Miscellaneous Topics on Chest Diseases.